

***Supplementary Information for***

**Synthesis, biological evaluation and induced fit docking simulation study  
of D-glucose-conjugated 1*H*-1,2,3-triazoles having 4*H*-pyrano[2,3-*d*]pyrimidine ring as potential agents against bacteria and fungi**

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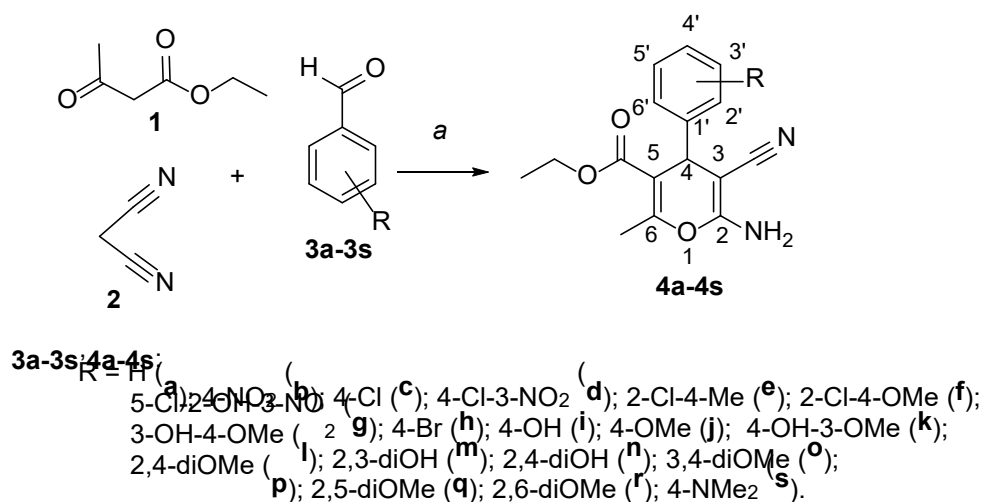
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## EXPERIMENTAL PART

Melting points were determined by open capillary method on STUART SMP3 (BIBBY STERILIN, UK). The IR spectra were recorded on FT-IR Affinity-1S Spectrometer (Shimadzu, Japan) in KBr pellet. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on Avance AV500 Spectrometer (Bruker, Germany) at 500 MHz and 125 MHz, respectively, using  $\text{DMSO-}d_6$  as solvent and TMS as an internal standard. ESI-mass spectra were recorded on LC-MS LTQ Orbitrap XL, ESI/HR-mass spectra were recorded on Thermo Scientific Exactive Plus Orbitrap spectrometers (ThermoScientific, USA) in methanol using ESI method. The analytical thin-layer chromatography (TLC) was performed on silica gel 60 WF<sub>254</sub>S aluminum sheets (Merck, Germany) and was visualized with UV light or by iodine vapor. Chemical reagents in high purity were purchased from the Merck Chemical Company (in Viet Nam). All materials were of reagent grade for organic synthesis. Ethyl ester of 2-amino-3-cyano-4-(substituted-phenyl)-4*H*-pyran-3-carboxylic acids **4a-4s** were prepared by using previous procedure [1], but THEAA was used as the catalyst under ultrasound-assisted conditions (*see below*). The corresponding 4*H*-pyrano[2,3-*d*]pyrimidines **5a-5s** were synthesized by modified previous procedures [1], while TFA was applied as a catalyst instead concentrated sulfuric acid (*see below*).

### 1. General procedure for synthesis of ethyl 6-amino-5-cyano-2-methyl-4-(substituted phenyl)-4*H*-pyran-3-carboxylates (**4a-4s**)



Scheme 1S. Synthesis of compounds **4a-4s**.

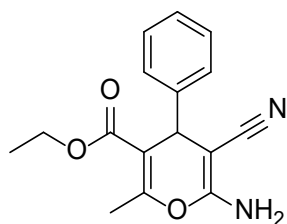
Ionic liquid tri-(2-hydroxyethyl)ammonium acetate [<sup>+</sup>HN(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub>][<sup>-</sup>OAc] (THEAA) was prepared by neutralization of ethanolamine in ethanol with glacial acetic acid.

Triethanolamine (0.5 mol, 74.5 g) was dissolved in 100 mL of absolute ethanol to form a liquid mixture. This mixture was placed in a water bath of 25°C and equipped with a reflux condenser under vigorous stirring with a magnetic stirrer. A solution of acetic acid (0.5 mol) in absolute ethanol (100 mL) was added dropwise to the flask in about 90 min. The reaction lasted for 2 h. The solvent was removed by evaporation under reduced pressure. The resulting crude residue was dried under vacuum at 50°C for 48 h.

To a solution of ethyl acetoacetate **1** (5 mmol, 0.77g, 0.7 mL), malononitrile **2** (5 mmol, 0.33 g, 0.31 mL) and appropriate substituted benzaldehyde **3a-3s** (5 mmol) in 96% ethanol (10 mL) was added THEAA (5 mol%, 1.57 g). The reaction mixture was stirred at 25 °C for 20 min. The separated solid product was filtered, washed by water and recrystallized from 96% ethanol to afford the titled ethyl ester **4a-4s** of 4*H*-pyran-3-carbonitriles.

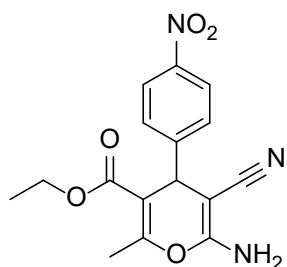
Some selected compounds are as follows.

*Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate (4a)*



White solids, from **3a** (R = H, 5 mmol, 530 mg, 0.51 mL). Yield: 1.35 g (95%). M.p.: 195–196 °C; refs. [2]: 195–196 °C; [3]: 194–196 °C; [4]:194–196 °C; [5]: 195–196 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.32 (t, *J* = 7.5 Hz, 2H, H-3 & H-5 phenyl), 7.23 (d, *J* = 7.5 Hz, 1H, H-4'), 7.15 (d, *J* = 7.1 Hz, 2H, H-2 & H-6 phenyl), 6.91 (s, 2H, 6-NH<sub>2</sub>), 4.30 (s, 1H, H-4), 4.01–3.94 (m, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.32 (s, 3H, 2-CH<sub>3</sub>), 1.04 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

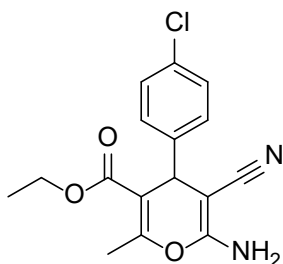
*Ethyl 6-amino-5-cyano-2-methyl-4-(4-nitrophenyl)-4H-pyran-3-carboxylate (4b)*



Pale yellow solids, from **3b** (R = 4-NO<sub>2</sub>, 5 mmol, 755 mg). Yield: 1.48 g (90%). M.p.: 180–181 °C; refs. [2]: 182–183 °C; [4]: 180–183 °C; [5]: 180–183 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 8.21 (d, *J* = 8.75 Hz, 2H, H-3 & H-5 phenyl), 7.46 (d, *J* = 8.75 Hz, 2H, H-2 & H-6 phenyl), 7.09 (s, 2H, 6-NH<sub>2</sub>), 4.49 (s, 1H, H-4), 4.00–3.94 (m, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>),

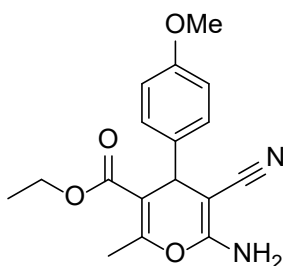
2.37 (s, 3H, 2-CH<sub>3</sub>), 1.03 (t,  $J= 7.25$  Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 6-amino-5-cyano-2-methyl-4-(4-chlorophenyl)-4H-pyran-3-carboxylate (4c)*



White solids, from **3c** (R = 4-Cl, 5 mmol, 703 mg). Yield: 1.43 g (90%). M.p.: 170–172 °C; refs. [2]: 172–174 °C; [4]: 171–173 °C; [5]: 172–174 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  (ppm): 7.38 (d,  $J= 8.50$  Hz, 2H, H-3 & H-5 phenyl), 7.18 (d,  $J= 8.50$  Hz, 2H, H-2 & H-6 phenyl), 6.96 (s, 2H, 6-NH<sub>2</sub>), 4.32 (s, 1H, H-4), 4.03–3.92 (m, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.32 (s, 3H, 2-CH<sub>3</sub>), 1.05 (t,  $J= 7.25$  Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

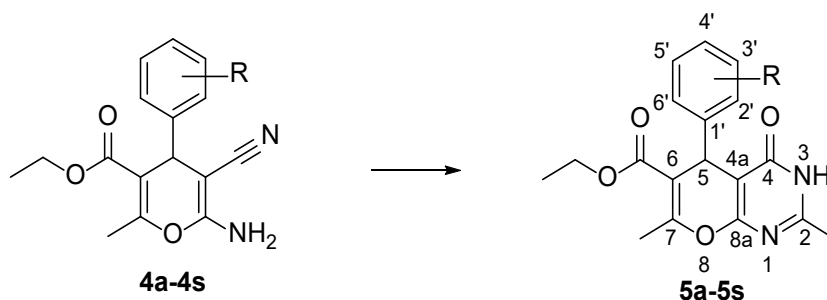
*Ethyl 6-amino-5-cyano-2-methyl-4-(4-methoxyphenyl)-4H-pyran-3-carboxylate (4j)*



White solids, from **3j** (R = 4-OMe, 5 mmol, 680 mg, 0.61 mL). Yield: 1.38 g (88%). M.p.: 142–142 °C; refs. [2]: 142–144 °C; [3]: 221–222 °C; [4]: 141–143 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  (ppm): 6.87 (d,  $J= 8.5$  Hz, 2H, H-3 & H-5 phenyl), 7.06 (d,  $J= 8.5$  Hz, 2H, H-2 & H-6 phenyl), 6.86 (s, 2H, 6-NH<sub>2</sub>), 4.25 (s, 1H, H-4), 4.03–3.93 (m, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.29 (s, 3H, 2-CH<sub>3</sub>), 1.07 (t,  $J= 7.0$  Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.73 (s, 3H, 4-OCH<sub>3</sub> phenyl).

## 2. General procedure for synthesis of ethyl 2,7-dimethyl-5-(substituted phenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-*d*]pyrimidine-6-carboxylates (5a-5s)



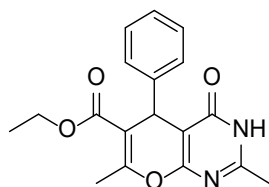


**4a-4s; 5a-5s;**  
 R = H (**a**); 2-NO<sub>2</sub> (**b**); 4-Cl (**c**); 4-Cl-3-NO<sub>2</sub> (**d**); 2-Cl-4-Me (**e**); 2-Cl-4-OMe (**f**);  
 3-OH-4-OMe (**g**); 4-Br (**h**); 4-OH (**i**); 4-OMe (**j**); 4-OH-3-OMe (**k**);  
 2,4-diOMe (**l**); 2,3-diOH (**m**); 2,4-diOH (**n**); 3,4-diOMe (**o**);  
 2,5-diOMe (**p**); 2,6-diOMe (**q**); 4-NMe<sub>2</sub> (**s**).

**Scheme 2S.** Synthesis of 4*H*-pyrano[2,3-*d*]pyrimidines **5a-5s**.

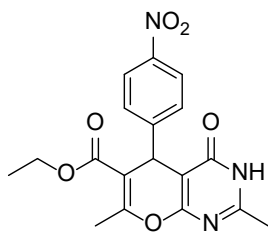
Reaction mixture of corresponding 4*H*-pyrans **4a-4s** (1 mmol), anhydride acetic (1.25 mL), and trifluoroacetic acid (0.025 mL) was heated under reflux at 100 °C for 15 min, then cooled to room temperature and left overnight (24 h). Upon completion, as monitored using TLC plates, the mixture was poured into cold water (10 mL). The crude product of 4*H*-pyrano[2,3-*d*]pyrimidine **5a-5s** was filtered, washed by water (3×2.5 mL), crystallized from 96% ethanol to afford compound **5a-5s**.

*Ethyl 2,7-dimethyl-5-phenyl-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5a)*



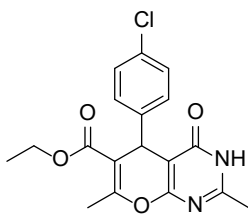
White solids, from **4a** (R = H, 2 mmol, 568 mg). Yield: 587 mg (90.3%). M.p.: 237–239 °C. Ref. [6, 7]: no physical and spectral data; [1]: 237–239 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.49 (s, 1H, 3-NH), 7.26 (t, *J* = 7.5 Hz, 2H, H-3 & H-5 phenyl), 7.22 (d, *J* = 1.5 Hz, 2H, H-2 & H-6 phenyl), 7.18–7.15 (m, 1H, H-4'), 4.79 (s, 1H, H-5), 4.05–4.01 (m, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.25 (s, 3H, 7-CH<sub>3</sub>), 1.12 (t, *J* = 7.5 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.1 (C=O ester), 162.4, 160.4, 159.1, 158.2, 144.5, 128.5, 128.4, 127.1, 108.4, 101.1, 60.7 (OCH<sub>2</sub>CH<sub>3</sub>), 36.3 (C-5), 21.5 (2-CH<sub>3</sub>), 18.8 (7-CH<sub>3</sub>), 14.3 (OCH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(4-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5b)*



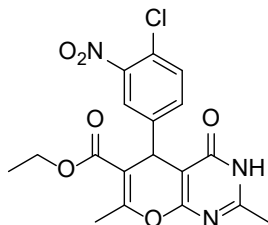
Ivory solids, from **4b** (R = 4-NO<sub>2</sub>, 2 mmol, 658 mg). Yield: 683 mg (92.2%). M.p.: 220–222 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.55 (s, 1H, 3-NH), 8.12 (t, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 7.50 (d, *J* = 8.5 Hz, 2H, H-2 & H-6 phenyl), 4.90 (s, 1H, H-5), 4.01 (q, *J* = 7.25 Hz, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.42 (s, 3H, 2-CH<sub>3</sub>), 2.25 (s, 3H, 7-CH<sub>3</sub>), 1.09 (t, *J* = 7.25 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 165.2 (C=O ester), 161.8, 159.9, 159.3, 159.3, 151.5, 146.2, 129.4, 123.3, 106.6, 99.5, 60.3 (OCH<sub>2</sub>CH<sub>3</sub>), 36.2 (C-5), 20.9 (2-CH<sub>3</sub>), 18.5 (7-CH<sub>3</sub>), 13.8 (OCH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(4-chlorophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5c)*



White solids, from **4c** (R = 4-Cl, 2 mmol, 637 mg). Yield: 668 mg (92.5%). M.p.: 235–237 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 7.33 (d, *J* = 8.25 Hz, 2H, H-3 & H-5 phenyl), 7.23 (d, *J* = 8.25 Hz, 2H, H-2 & H-6 phenyl), 6.77 (s, 1H, H-5), 4.05 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 165.9 (C=O ester), 162.4, 160.3, 159.8, 159.0, 143.5, 131.7, 130.4, 128.5, 107.8, 100.6, 60.7 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 36.0 (C-5), 21.4 (2-CH<sub>3</sub>), 18.9 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

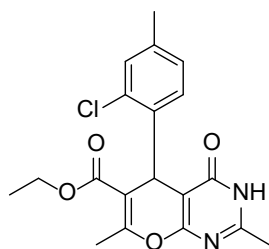
*Ethyl 2,7-dimethyl-5-(4-chloro-3-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5d)*



White solids, from **4d** (R = 4-Cl-3-NO<sub>2</sub>, 2 mmol, 727 mg). Yield: 729 mg (89%). M.p.: 225–227 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 8.16 (s, 1H, H-2 phenyl), 7.67 (d, *J* = 7.75 Hz, 1H, H-5 phenyl), 7.52 (d, *J* = 7.75 Hz, 1H, H-6 phenyl), 6.42 (s, 1H, H-5), 4.05 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>),

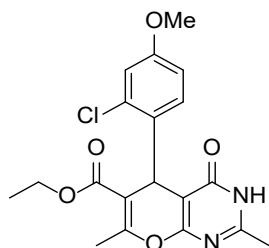
1.14 (t,  $J = 7.0$  Hz, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2-chloro-4-methylphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5e)*



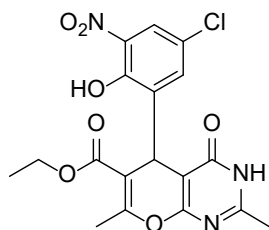
White solids, from **4e** (R = 2-Cl-4-Me, 2 mmol, 665 mg). Yield: 673 mg (90.2%). M.p.: 236–238 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  (ppm): 12.25 (s, 1H, 3-NH), 7.41 (s, 1H, H-3 phenyl), 7.28 (d,  $J = 8.5$  Hz, 1H, H-5 phenyl), 7.09 (d,  $J = 8.5$  Hz, 1H, H-6 phenyl), 6.15 (s, 1H, H-5), 4.05 (q,  $J = 7.0$  Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t,  $J = 7.0$  Hz, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2-chloro-4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5f)*



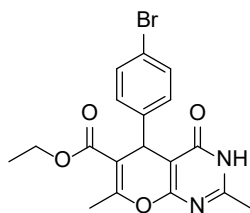
White solids, from **4f** (R = 2-Cl-4-OMe, 2 mmol, 697 mg). Yield: 688 mg (88.2%). M.p.: 223–225 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  (ppm): 12.25 (s, 1H, 3-NH), 7.27 (d,  $J = 9.0$  Hz, 1H, H-6 phenyl), 7.04 (s, 1H, H-3 phenyl), 6.40 (dd,  $J = 1.5, 8.5$  Hz, 1H, H-5 phenyl), 6.15 (s, 1H, H-5), 4.05 (q,  $J = 7.0$  Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.79 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t,  $J = 7.0$  Hz, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(5-chloro-2-hydroxy-3-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5g)*



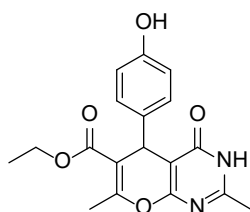
White solids, from **4f** (R = 5-Cl-2-OH-3-NO<sub>2</sub>, 2 mmol, 759 mg). Yield: 734 mg (87.1%). M.p.: 225–227 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>),  $\delta$  (ppm): 12.25 (s, 1H, 3-NH), 11.77 (s, 1H, 2-OH phenyl), 7.02 (s, 1H, H-4 phenyl), 7.51 (s, 1H, H-6 phenyl), 6.39 (s, 1H, H-5), 4.05 (q,  $J = 7.0$  Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.79 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.31 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t,  $J = 7.0$  Hz, 3H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

Ethyl 2,7-dimethyl-5-(4-bromophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (**5h**)



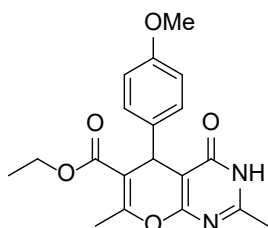
White solids, from **4h** (R = 4-Br, 2 mmol, 726 mg). Yield: 747 mg (92.5%). M.p.: 263–265 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 7.54 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 7.31 (d, *J* = 8.5 Hz, 2H, H-2 & H-6 phenyl), 6.15 (s, 1H, H-5), 4.05 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.12 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 165.4, 161.9, 159.8, 158.8, 158.5, 143.4, 130.9, 130.3, 119.7, 107.3, 100.1, 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 35.6 (C-5), 20.9 (2-CH<sub>3</sub>), 18.4 (7-CH<sub>3</sub>), 13.8 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

Ethyl 2,7-dimethyl-5-(4-hydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (**5i**)



White solids, from **4i** (R = 4-OH, 2 mmol, 600 mg). Yield: 600 mg (87.7%). M.p.: 251–253 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 8.36 (s, 1H, 4'-OH), 7.04 (d, *J* = 8.0 Hz, 2H, H-2 & H-6 phenyl), 6.64 (d, *J* = 8.0 Hz, 2H, H-3 & H-5 phenyl), 6.15 (s, 1H, H-5), 4.04 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.8 (C=O ester), 162.8, 159.4, 158.8, 157.5, 155.7, 136.7, 129.1, 114.4, 108.9, 97.9, 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 36.3 (C-5), 20.5 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

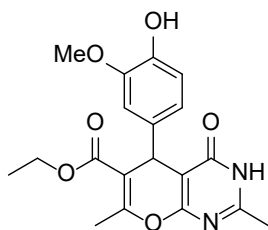
Ethyl 2,7-dimethyl-5-(4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (**5j**)



White solids, from **4j** (R = 4-OMe, 2 mmol, 628 mg). Yield: 648 mg (91.1%). M.p.:

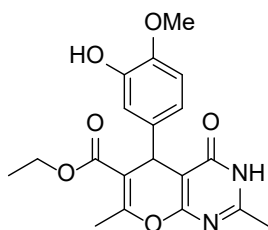
224–226 °C. Ref. [8]: no physical and spectral data. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 7.16 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 6.87 (d, *J* = 8.5 Hz, 2H, H-2 & H-6 phenyl), 6.15 (s, 1H, H-5), 4.03 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.78 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.39 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.2 (C=O ester), 162.4, 160.3, 158.9, 158.4, 158.2, 136.7, 129.4, 113.9, 108.6, 101.3, 60.6 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 55.5 (4-OCH<sub>3</sub> phenyl), 35.5 (C-5), 21.4 (2-CH<sub>3</sub>), 18.8 (7-CH<sub>3</sub>), 14.4 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(4-hydroxy-3-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5k)*



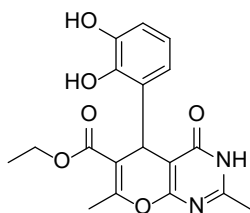
White solids, from **4k** (R = 4-OH-3-OMe, 2 mmol, 667 mg). Yield: 663 mg (90.2%). M.p.: 276–278 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 7.76 (s, 1H, 4-OH phenyl), 6.85–6.81 (m, 2H, H-5 & H-6 phenyl), 6.71 (s, 1H, H-2 phenyl), 6.14 (s, 1H, H-5), 4.05 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.78 (s, 3H, 3'-OCH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(3-hydroxy-4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5l)*



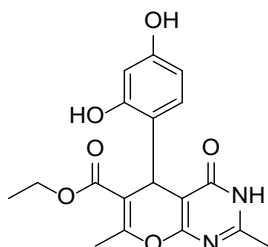
White solids, from **4l** (R = 3-OH-4-OMe, 2 mmol, 660 mg). Yield: 667 mg (89.5%); M.p.: 248–249 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 6.91 (s, 3-OH phenyl), 6.89 (d, *J* = 8.5 Hz, 1H, H-5 phenyl), 6.81 (d, *J* = 8.5 Hz, 1H, H-6 phenyl), 6.07 (s, 1H, H-5), 4.03 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.82 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,3-dihydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5m)*



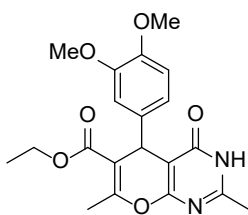
White solids, from **4m** (R = 2,3-diOH, 2 mmol, 632 mg). Yield: 634 mg (88.6%); M.p.: 245–247 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.47 (s, 1H, 3-NH), 8.40 (s, 1H, 3-OH phenyl), 7.76 (s, 1H, 2-OH phenyl), 6.92–6.87 (m, 2H, H-5 & H-6 phenyl), 5.98 (s, 1H, H-5), 5.76–5.74 (m, 1H, H-4 phenyl), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 3.70 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,4-dihydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5n)*



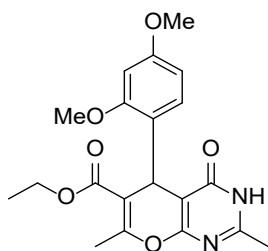
White solids, from **4n** (R = 2,4-diOH, 2 mmol, 632 mg). Yield: 639 mg (89.3%); M.p.: 250–252 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.54 (s, 1H, 3-NH), 8.33 (s, 1H, 2-OH phenyl), 7.91 (s, 1H, 4-OH phenyl), 7.14 (d, *J* = 8.5 Hz, 1H, H-6 phenyl), 6.45 (dd, *J* = 2.0, 8.5 Hz, 1H, H-5 phenyl), 6.35 (d, *J* = 2.0 Hz, 1H, H-3 phenyl), 6.11 (s, 1H, H-5), 5.76–5.74 (m, 1H, H-4 phenyl), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(3,4-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5o)*



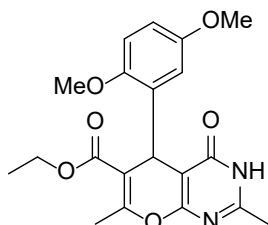
White solids, from **4o** (R = 3,4-diOMe, 2 mmol, 688 mg). Yield: 704 mg (91.2%). M.p.: 265–267 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 6.93–6.89 (m, 2H, H-2 & H-3 phenyl), 6.81 (s, 1H, H-6 phenyl), 6.14 (s, 1H, H-5), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 3.80 (s, 3H, 3-OCH<sub>3</sub>), 3.74 (s, 3H, 4-OCH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,4-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5p)*



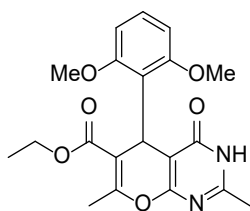
White solids, from **4p** (R = 2,4-diOMe, 2 mmol, 688 mg). Yield: mg 689 (89.3%); M.p.: 246–248 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 6.93 (d, *J* = 8.5 Hz, 1H, H-6 phenyl), 6.57 (s, 1H, H-3 phenyl), 6.44 (d, *J* = 8.5 Hz, 1H, H-5 phenyl), 6.14 (s, 1H, H-5), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 3.83 (s, 3H, 2-OCH<sub>3</sub>), 3.79 (s, 3H, 4-OCH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,5-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5q)*



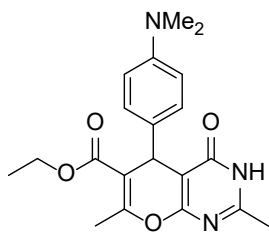
White solids, from **4q** (R = 2,5-diOMe, 2 mmol, 688 mg). Yield: mg 691 (89.5%); M.p.: 239–240 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 6.95 (s, 1H, H-6 phenyl), 6.94 (d, *J* = 8.5 Hz, 1H, H-3 phenyl), 6.81 (d, *J* = 8.5 Hz, 1H, H-4 phenyl), 6.08 (s, 1H, H-5), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 3.82 (s, 3H, 2-OCH<sub>3</sub>), 3.78 (s, 3H, 5-OCH<sub>3</sub>), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,6-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5r)*



White solids, from **4r** (R = 2,6-diOMe, 2 mmol, 688 mg). Yield: 696 mg (90.1%); M.p.: 253–255 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.25 (s, 1H, 3-NH), 7.22 (t, *J* = 8.5 Hz, 1H, H-4 phenyl), 6.50 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 6.20 (s, 1H, H-5), 4.03 (q, *J* = 7.0 Hz, 2H, COOCH<sub>2</sub>CH<sub>3</sub>), 3.83 (s, 6H, 2-OCH<sub>3</sub> & 6-OCH<sub>3</sub> phenyl), 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

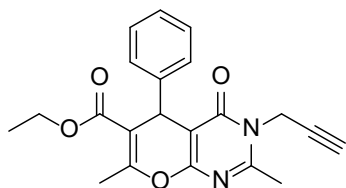
*Ethyl 2,7-dimethyl-5-(4-dimethylaminophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5s)*



White solids, from **4p** (R = 4-NMe<sub>2</sub>, 2 mmol, 654 mg). Yield: 664 mg (90.2%). M.p.: 244–246 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 12.53 (s, 1H, 3-NH), 7.07 (d, *J* = 8.5 Hz, 2H, H-2 & H-6 phenyl), 6.60 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 6.15 (s, 1H, H-5), 4.05 (q, *J* = 7.0 Hz, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.98 [4'-N(CH<sub>3</sub>)<sub>2</sub>], 2.40 (s, 3H, 2-CH<sub>3</sub>), 2.25 (s, 3H, 7-CH<sub>3</sub>), 1.12 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.8 (C=O ester), 162.8, 159.3, 158.8, 157.5, 149.5, 135.7, 128.6, 112.3, 108.9, 97.9, 60.2 (OCH<sub>2</sub>CH<sub>3</sub>), 40.3 [4'-N(CH<sub>3</sub>)<sub>2</sub>], 35.5 (C-5), 20.5 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (OCH<sub>2</sub>CH<sub>3</sub>).

### 3. Physical and spectral data of ethyl 2,7-dimethyl-5-(substituted phenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-*d*]pyrimidine-6-carboxylates (**6a-6p**)

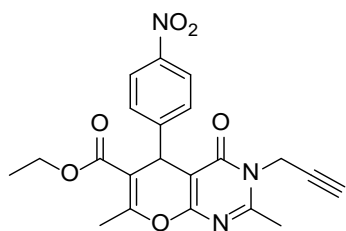
*Ethyl 2,7-dimethyl-5-phenyl-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-*d*]pyrimidine-6-carboxylate (6a)*



White solids, from **5a** (R = H, 1 mmol, 326 mg). Yield: 348 mg (95.7%). M.p.: 131–132 °C; ref. [7]: no physical and spectral data; ref. [8]: 131–133 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.29–7.25 (m, 2H, H-3 & H-5 phenyl), 7.23 (d, *J* = 6.8 Hz, 2H, H-2 & H-6 phenyl), 7.16 (dd, *J* = 4.25, 9.75 Hz, 1H, H-4 phenyl), 4.83–4.72 (m, 1H, N-CH<sub>2</sub>C≡CH), 4.82 (s, 1H, H-5), 4.03 (qd, *J* = 7.0, 2.2 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.34 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.58 (s, 3H, 2-CH<sub>3</sub>), 2.42 (s, 3H, 7-CH<sub>3</sub>), 1.11 (t, *J* = 7.1 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.0 (C=O ester), 160.7, 159.7, 158.7, 158.5, 144.2, 128.6, 128.6, 127.2, 108.4, 100.7, 78.2 (N-CH<sub>2</sub>C≡CH), 75.6 (N-CH<sub>2</sub>C≡CH), 60.7 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 37.1 (C-5), 33.4 (N-CH<sub>2</sub>C≡CH), 22.6 (2-CH<sub>3</sub>), 18.8 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>, calc. for M+H = 365.1496 Da, M+Na = 387.1315 Da; found: *m/z* 365.1485 [M+H]<sup>+</sup>; 387.1342 [M+Na]<sup>+</sup>.

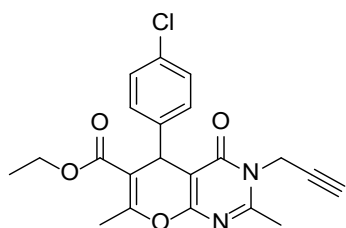
*Ethyl 2,7-dimethyl-5-(4-nitrophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-*d*]pyrimidine-6-carboxylate (6b)*





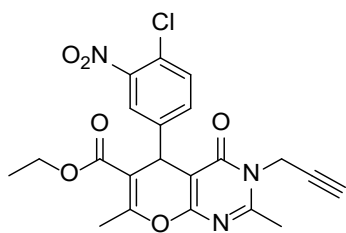
Ivory solids, from **5b** (R = 4-NO<sub>2</sub>, 1 mmol, 371 mg). Yield: 370 mg (90.5%). M.p.: 191–193 °C; ref. [8]: no physical and spectral data. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 8.08 (d, *J* = 8.0 Hz, 2H, H-3 & H-5 phenyl), 7.52 (d, *J* = 8.0 Hz, 2H, H-2 & H-6 phenyl), 6.13 (s, 1H, H-5), 5.15 (d, *J* = 2.0 Hz, 2H, N-CH<sub>2</sub>C≡CH), 4.03 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (m, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.9 (C=O ester), 161.8, 159.4, 158.7, 158.2, 147.5, 146.5, 128.4, 123.6, 108.8, 98.5, 78.0 (N-CH<sub>2</sub>C≡CH), 72.7 (N-CH<sub>2</sub>C≡CH), 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 38.1 (C-5), 33.2 (N-CH<sub>2</sub>C≡CH), 20.8 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>21</sub>H<sub>19</sub>N<sub>3</sub>O<sub>6</sub>, calc. for M+H = 410.1347 Da, M+Na = 432.1166 Da; found: *m/z* 410.1368 [M+H]<sup>+</sup>; 432.1189 [M+Na]<sup>+</sup>.

*Ethyl 2,7-dimethyl-5-(4-chlorophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6c)*



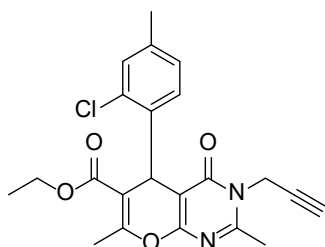
Ivory solids, from **5c** (R = 4-Cl, 1 mmol, 361 mg). Yield: 357 mg (89.5%). M.p.: 165–167 °C; ref. [8]: no physical and spectral data. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.33 (d, *J* = 8.4 Hz, 2H, H-3 & H-5 phenyl), 7.25 (d, *J* = 8.4 Hz, 2H, H-2 & H-6 phenyl), 4.82 (dd, *J* = 18.0, 2.5 Hz, 1H, N-CH<sub>2</sub><sup>(a)</sup>C≡CH), 4.80 (s, 1H, H-5), 4.71 (dd, *J* = 18.0, 2.5 Hz, 1H, N-CH<sub>2</sub><sup>(b)</sup>C≡CH), 4.92–4.77 (m, 2H, N-CH<sub>2</sub>C≡CH), 4.03 (dt, *J* = 12.7, 6.3 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.34 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.58 (s, 3H, 2-CH<sub>3</sub>), 2.42 (s, 3H, 7-CH<sub>3</sub>), 1.11 (t, *J* = 7.1 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 165.8 (C=O ester), 160.7, 159.9, 158.9, 158.7, 143.2, 131.8, 130.5, 128.6, 107.9, 100.3, 78.1 (N-CH<sub>2</sub>C≡CH), 75.6 (N-CH<sub>2</sub>C≡CH), 60.8 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 36.7 (C-5), 33.4 (N-CH<sub>2</sub>C≡CH), 22.6 (2-CH<sub>3</sub>), 18.9 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>21</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>4</sub>, calc. for M+H/M+H+2 = 399.1106/401.1077 Da (with <sup>35</sup>Cl/<sup>37</sup>Cl); found: *m/z* 399.1127 [M+H]<sup>+</sup>, 401.1049 [M+H+2]<sup>+</sup>.

*Ethyl 2,7-dimethyl-5-(4-chloro-3-nitrophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6d)*



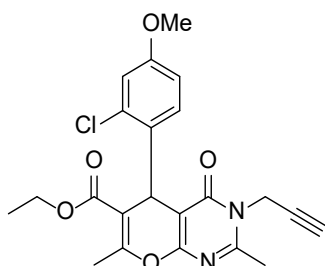
Pale yellow solids, from **5d** (R = 4-Cl-3-NO<sub>2</sub>, 1 mmol, 406 mg). Yield: 391 mg (88.1%). M.p.: 128–130 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 8.16 (s, 1H, H-2 phenyl), 7.67 (d, *J* = 7.75 Hz, 1H, H-5 phenyl), 7.51 (d, *J* = 7.75 Hz, 1H, H-6 phenyl), 6.40 (s, 1H, H-5), 5.15 (s, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.64 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2-chloro-4-methylphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6e)*



White solids, from **5e** (R = 2-Cl-4-Me, 1 mmol, 375 mg). Yield: 369 mg (89.4%). M.p.: 136–138 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.41 (s, 1H, H-3 phenyl), 7.28 (d, *J* = 8.5 Hz, 1H, H-5 phenyl), 7.09 (d, *J* = 8.5 Hz, 1H, H-6 phenyl), 6.13 (s, 1H, H-5), 5.15 (s, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

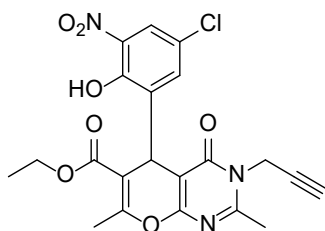
*Ethyl 2,7-dimethyl-5-(2-chloro-4-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6f)*



White solids, from **5f** (R = 2-Cl-4-OMe, 1 mmol, 391mg). Yield: 379 mg (88.5%). M.p.: 123–125 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.27 (d, *J* = 8.75 Hz, 1H, H-5 phenyl), 7.03 (d, *J* = 1.5 Hz, 1H, H-3 phenyl), 6.84 (dd, *J* = 1.5, 8.75 Hz, 1H, H-5 phenyl), 6.13 (s, 1H, H-5), 5.14 (d, *J* = 2.0 Hz, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.79 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

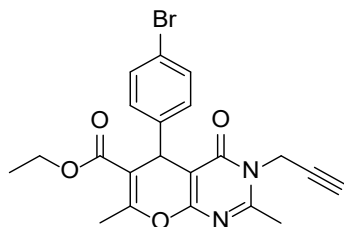
*Ethyl 2,7-dimethyl-5-(5-chloro-2-hydroxy-3-nitrophenylphenyl)-4-oxo-3-propargyl-3,5-*

*dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6g)*



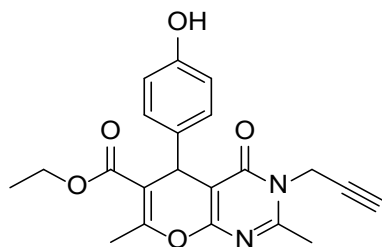
White solids, from **5f** (R = 5-Cl-2-OH-3-NO<sub>2</sub>, 2 mmol, 422 mg). Yield: 412 mg (89.6%). M.p.: 143–145 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 11.77 (s, 1H, 2-OH phenyl), 8.02 (s, 1H, H-4 phenyl), 7.51 (s, 1H, H-6 phenyl), 6.37 (s, 1H, H-5), 5.14 (d, *J* = 2.0 Hz, N-CH<sub>2</sub>C≡CH), 4.05 (q, *J* = 7.0 Hz, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(4-bromophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6h)*



Ivory solids, from **5h** (R = 4-Br, 1 mmol, 405 mg). Yield: 380 mg (85.9%). M.p.: 193–195 °C; ref. [8]: no physical and spectral data. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.54 (d, *J* = 8.25 Hz, 2H, H-3 & H-5 phenyl), 7.25 (d, *J* = 8.25 Hz, 2H, H-2 & H-6 phenyl), 6.13 (s, 1H, H-5), 5.15 (s, 2H, N-CH<sub>2</sub>C≡CH), 4.03 (q, *J* = 7.0 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.0 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.8 (C=O ester), 161.8, 159.4, 158.7, 158.2, 141.9, 131.2, 128.8, 120.5, 108.8, 98.6, 78.0 (N-CH<sub>2</sub>C≡CH), 72.7 (N-CH<sub>2</sub>C≡CH), 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 36.7 (C-5), 33.2 (N-CH<sub>2</sub>C≡CH), 20.8 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>21</sub>H<sub>19</sub>BrN<sub>2</sub>O<sub>4</sub>, calc. for M+H/M+H+2 = 443.0601/445.0580 Da (with <sup>79</sup>Br/<sup>81</sup>Br); found: *m/z* 443.0632 [M+H]<sup>+</sup>, 445.0557 [M+H+2]<sup>+</sup>.

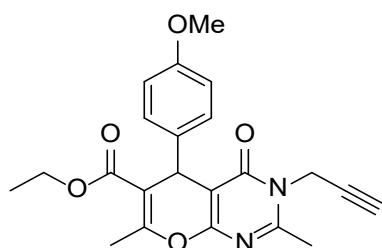
*Ethyl 2,7-dimethyl-5-(4-hydroxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6i)*



White solids, from **5i** (R = 4-OH, 1 mmol, 342 mg). Yield: 333 mg (87.7%). M.p.: 171–173 °C;

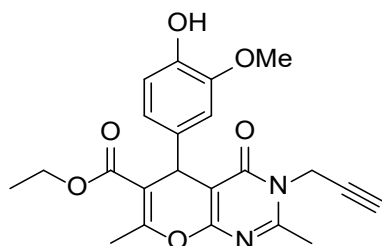
ref. [8]: no physical and spectral data.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 8.36 (s, 1H, 4-OH phenyl), 7.04 (d,  $J = 8.25$  Hz, 2H, H-2 & H-6 phenyl), 6.63 (d,  $J = 8.25$  Hz, 2H, H-3 & H-5 phenyl), 6.13 (s, 1H, H-5), 5.14 (s, 2H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 4.03 (q,  $J = 7.25$  Hz, 2H, 6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 2.83 (s, 1H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 2.65 (s, 3H, 2- $\text{CH}_3$ ), 2.29 (s, 3H, 7- $\text{CH}_3$ ), 1.14 (t,  $J = 7.0$  Hz, 3H, 6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 166.8 (C=O ester), 161.8, 159.4, 158.7, 158.2, 155.7, 136.2, 129.1, 114.4, 108.8, 98.6, 78.0 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 72.7 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 60.2 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 36.2 (C-5), 33.2 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 20.8 (2- $\text{CH}_3$ ), 19.5 (7- $\text{CH}_3$ ), 14.3 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ). ESI-HRMS(+):  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_5$ , calc. for  $\text{M}+\text{H} = 381.1445$  Da,  $\text{M}+\text{Na} = 403.1264$  Da; found:  $m/z$  381.1469  $[\text{M}+\text{H}]^+$ ; 403.1229  $[\text{M}+\text{Na}]^+$ .

*Ethyl 2,7-dimethyl-5-(4-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6j)*



White solids, from **5j** (R = 4-OMe, 1 mmol, 356 mg). Yield: 282 mg 318 mg (80.8%). M.p.: 147–149 °C. ref. [8]: 147–149 °C.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 7.13 (d,  $J = 8.75$  Hz, 2H, H-3 & H-5 phenyl), 6.82 (d,  $J = 8.75$  Hz, 2H, H-2 & H-6 phenyl), 4.82–4.72 (m, 1H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 4.76 (s, 1H, H-5), 4.04 (qd,  $J = 7.0$ , 1.4 Hz, 2H, 5- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 3.35 (s, 3H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 2.58 (s, 3H, 2- $\text{CH}_3$ ), 2.40 (s, 3H, 7- $\text{CH}_3$ ), 1.13 (t,  $J = 7.1$  Hz, 3H, 6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 3.70 (s, 3H, 4-OCH<sub>3</sub> phenyl).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 166.1 (C=O ester), 160.7, 159.5, 158.6, 158.5, 158.1, 136.3, 129.6, 114.0, 108.6, 101.0, 78.2 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 75.6 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 60.7 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 55.4 (4-OCH<sub>3</sub> phenyl), 36.2 (C-5), 33.3 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 22.6 (2- $\text{CH}_3$ ), 18.8 (7- $\text{CH}_3$ ), 14.3 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ). ESI-HRMS(+):  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_5$ , calc. for  $\text{M}+\text{H} = 395.1601$  Da,  $\text{M}+\text{Na} = 417.1421$  Da; found:  $m/z$  395.1633  $[\text{M}+\text{H}]^+$ ; 417.1451  $[\text{M}+\text{Na}]^+$ .

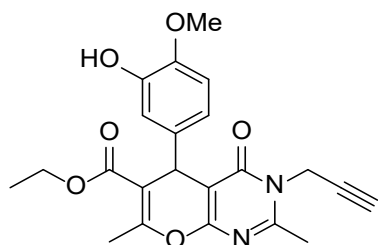
*Ethyl 2,7-dimethyl-5-(4-hydroxy-3-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6k)*



White solids, from **5k** (R = 4-OH-3-OMe, 1 mmol, 372 mg). Yield: 367 mg (89.5%). M.p.:

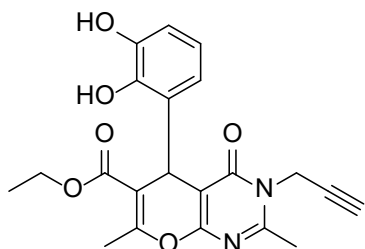
161–163 °C; ref. [8]: no physical and spectral data.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 7.76 (s, 1H, 4-OH phenyl), 6.85–6.82 (m, 2H, H-5 & H-6 phenyl), 6.71 (s, 1H, H-2 phenyl), 6.12 (s, 1H, H-5), 5.15 (s, 2H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 4.04 (q,  $J = 7.25$  Hz, 2H, 6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 3.78 (s, 3H, 3- $\text{OCH}_3$  phenyl), 2.83 (s, 1H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 2.65 (s, 3H, 2- $\text{CH}_3$ ), 2.30 (s, 3H, 7- $\text{CH}_3$ ), 1.13 (t,  $J = 7.25$  Hz, 3H, 6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 166.9 (C=O ester), 161.7, 159.4, 158.7, 158.2, 147.6, 145.2, 134.4, 122.2, 115.1, 111.8, 108.4, 98.8, 78.0 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 72.7 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 60.2 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 56.1 (3- $\text{OCH}_3$  phenyl), 38.6 (C-5), 33.2 (N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 20.8 (2- $\text{CH}_3$ ), 19.5 (7- $\text{CH}_3$ ), 14.3 (6- $\text{CO}_2\text{CH}_2\text{CH}_3$ ). ESI-HRMS(+):  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_6$ , calc. for  $\text{M}+\text{H} = 411.1551$  Da,  $\text{M}+\text{Na} = 433.1370$  Da; found:  $m/z$  411.1579  $[\text{M}+\text{H}]^+$ ; 433.1345  $[\text{M}+\text{Na}]^+$ .

*Ethyl 2,7-dimethyl-5-(3-hydroxy-4-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5l)*



White solids, from **4l** (R = 3-OH-4-OMe, 1 mmol, 372 mg). Yield: 365 mg (89.2%); M.p.: 148–149 °C.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 7.60 (s, 1H, 3-OH phenyl), 6.91 (s, 1H, H-2 phenyl), 6.89 (d,  $J = 8.5$  Hz, 1H, H-5 phenyl), 6.81 (d,  $J = 8.5$  Hz, 1H, H-6 phenyl), 6.05 (s, 1H, H-5), 5.15 (s, 2H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 4.05 (q,  $J = 7.0$  Hz, 2H, 5- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 3.82 (s, 3H, 4- $\text{OCH}_3$  phenyl), 2.83 (s, 1H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 2.65 (s, 3H, 2- $\text{CH}_3$ ), 2.29 (s, 3H, 7- $\text{CH}_3$ ), 1.13 (t,  $J = 7.0$  Hz, 3H, 5- $\text{CO}_2\text{CH}_2\text{CH}_3$ ).

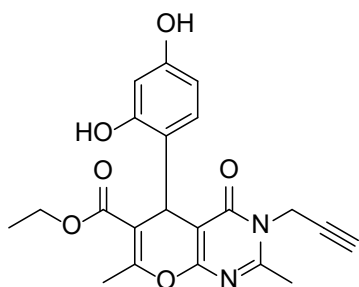
*Ethyl 2,7-dimethyl-5-(2,3-dihydroxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5m)*



White solids, from **4m** (R = 2,3-diOH, 1 mmol, 358 mg). Yield: 350 mg (88.5%); M.p.: 155–157 °C.  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ ),  $\delta$  (ppm): 8.40 (s, 1H, 3-OH phenyl), 7.76 (s, 1H, 2-OH phenyl), 6.91 (d,  $J = 7.75$  Hz, 1H, H-6 phenyl), 6.89 (t,  $J = 7.75$  Hz, 1H, H-5 phenyl), 5.96 (s, 1H, H-5), 5.75 (d,  $J = 7.75$  Hz, 1H, H-4 phenyl), 5.15 (s, 2H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 4.05 (q,  $J = 7.0$  Hz, 2H, 5- $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 3.82 (s, 3H, 4- $\text{OCH}_3$  phenyl), 2.83 (s, 1H, N- $\text{CH}_2\text{C}\equiv\text{CH}$ ), 2.65 (s, 3H, 2- $\text{CH}_3$ ), 2.29 (s, 3H, 7- $\text{CH}_3$ ), 1.13 (t,  $J = 7.0$  Hz, 3H, 5- $\text{CO}_2\text{CH}_2\text{CH}_3$ ).

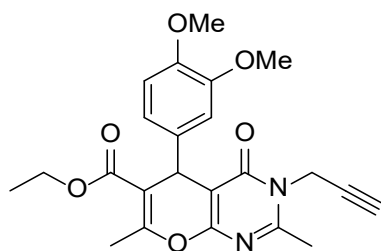
*Ethyl 2,7-dimethyl-5-(2,4-dihydroxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-*

*d*]pyrimidine-6-carboxylate (**5n**)



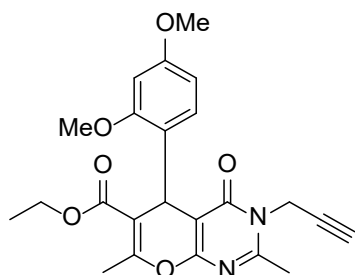
White solids, from **4n** (R = 2,4-diOH, 1 mmol, 358 mg). Yield: 353 mg (89.2%); M.p.: 178–179 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 8.33 (s, 1H, 2-OH phenyl), 7.91 (s, 1H, 4-OH phenyl), 7.13 (d, *J* = 9.0 Hz, 1H, H-6 phenyl), 6.45 (dd, *J* = 1.75, 8.5 Hz, 1H, H-5 phenyl), 6.35 (d, *J* = 1.75 Hz, 1H, H-3 phenyl), 6.09 (s, 1H, H-5), 5.14 (d, *J* = 2.0 Hz, N-CH<sub>2</sub>C≡CH), 4.05 (q, *J* = 7.0 Hz, 2H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.82 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.13 (t, *J* = 7.0 Hz, 3H, 5-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(3,4-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6o)*



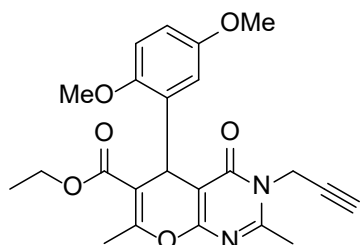
White solids, from **5o** (R = 3,4-diOMe, 1 mmol, 386 mg). Yield: 371 mg (87.4%). M.p.: 142–144 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 6.93–6.89 (m, 2H, H-5 & H-6 phenyl), 6.81 (s, 1H, H-2 phenyl), 6.12 (s, 1H, H-5), 5.15 (d, *J* = 2.0 Hz, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.80 (s, 3H, 3-OCH<sub>3</sub> phenyl), 3.74 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.9 (C=O ester), 161.7, 159.4, 158.7, 158.2, 149.2, 148.3, 135.8, 122.1, 113.1, 112.1, 108.3, 98.8, 78.0 (N-CH<sub>2</sub>C≡CH), 72.7 (N-CH<sub>2</sub>C≡CH), 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 55.91 (4-OCH<sub>3</sub> phenyl), 55.89 (3-OCH<sub>3</sub> phenyl), 38.6 (C-5), 33.2 (N-CH<sub>2</sub>C≡CH), 20.8 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>23</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>, calc. for M+H = 425.1707 Da, M+Na = 447.1527 Da; found: *m/z* 425.1728 [M+H]<sup>+</sup>; 447.1552 [M+Na]<sup>+</sup>.

*Ethyl 2,7-dimethyl-5-(2,4-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5p)*



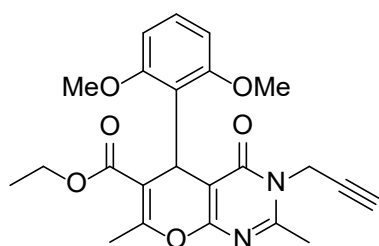
White solids, from **4p** (R = 2,4-diOMe, 1 mmol, 386 mg). Yield: 370 mg (87.2%); M.p.: 146–148 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 6.93 (d, *J* = 8.0 Hz, 1H, H-6 phenyl), 6.57 (d, *J* = 1.5 Hz, 1H, H-3 phenyl), 6.45 (dd, *J* = 1.5, 8.0 Hz, 1H, H-5 phenyl), 6.12 (s, 1H, H-5), 5.14 (d, *J* = 2.0 Hz, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.83 (s, 3H, 2-OCH<sub>3</sub> phenyl), 3.79 (s, 3H, 4-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(2,5-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5q)*



White solids, from **4q** (R = 2,5-diOMe, 2 mmol, 688 mg). Yield: 368 mg (86.9%); M.p.: 135–137 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 6.95 (s, 1H, H-6 phenyl), 6.94 (d, *J* = 7.75 Hz, 1H, H-3 phenyl), 6.81 (dd, *J* = 1.5, 7.75 Hz, 1H, H-4 phenyl), 6.05 (s, 1H, H-5), 5.14 (d, *J* = 2.0 Hz, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.82 (s, 3H, 2-OCH<sub>3</sub> phenyl), 3.78 (s, 3H, 5-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.64 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.14 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

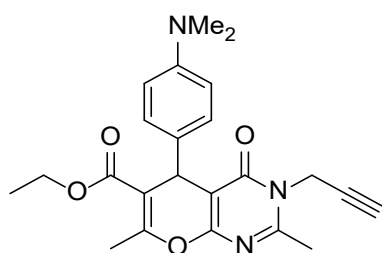
*Ethyl 2,7-dimethyl-5-(2,6-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (5r)*



White solids, from **4r** (R = 2,6-diOMe, 2 mmol, 688 mg). Yield: 366 mg (86.3%); M.p.: 157–159 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.21 (t, *J* = 8.5 Hz, 1H, H-4 phenyl), 6.50 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 6.18 (s, 1H, H-5), 5.15 (s, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.83 (s, 6H, 2-OCH<sub>3</sub> & 6-OCH<sub>3</sub> phenyl), 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.29 (s, 3H, 7-CH<sub>3</sub>), 1.13 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

*Ethyl 2,7-dimethyl-5-(4-dimethylaminophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-*

pyrano[2,3-d]pyrimidine-6-carboxylate (**6s**)



White solids, from **5s** (R = 4-NMe<sub>2</sub>, 1 mmol, 369 mg). Yield: 332 mg (81.7%). M.p.: 155–157 °C. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 7.07 (d, *J* = 8.5 Hz, 2H, H-2 & H-6 phenyl), 6.60 (d, *J* = 8.5 Hz, 2H, H-3 & H-5 phenyl), 6.13 (s, 1H, H-5), 5.15 (s, 2H, N-CH<sub>2</sub>C≡CH), 4.04 (q, *J* = 7.25 Hz, 2H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.98 [s, 6H, 4-N(CH<sub>3</sub>)<sub>2</sub> phenyl], 2.83 (s, 1H, N-CH<sub>2</sub>C≡CH), 2.65 (s, 3H, 2-CH<sub>3</sub>), 2.30 (s, 3H, 7-CH<sub>3</sub>), 1.13 (t, *J* = 7.25 Hz, 3H, 6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>), δ (ppm): 166.8 (C=O ester), 161.8, 159.4, 158.7, 158.2, 149.5, 135.5, 128.6, 112.3, 108.8, 98.6, 78.0 (N-CH<sub>2</sub>C≡CH), 72.7 (N-CH<sub>2</sub>C≡CH), 60.2 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 40.3 [4-N(CH<sub>3</sub>)<sub>2</sub> phenyl], 37.2 (C-5), 33.2 (N-CH<sub>2</sub>C≡CH), 20.8 (2-CH<sub>3</sub>), 19.5 (7-CH<sub>3</sub>), 14.3 (6-CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>). ESI-HRMS(+): C<sub>23</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>, calc. for M+H = 408.1918 Da, M+Na = 430.1737 Da; found: *m/z* 408.1942 [M+H]<sup>+</sup>; 430.1754 [M+Na]<sup>+</sup>.

## References

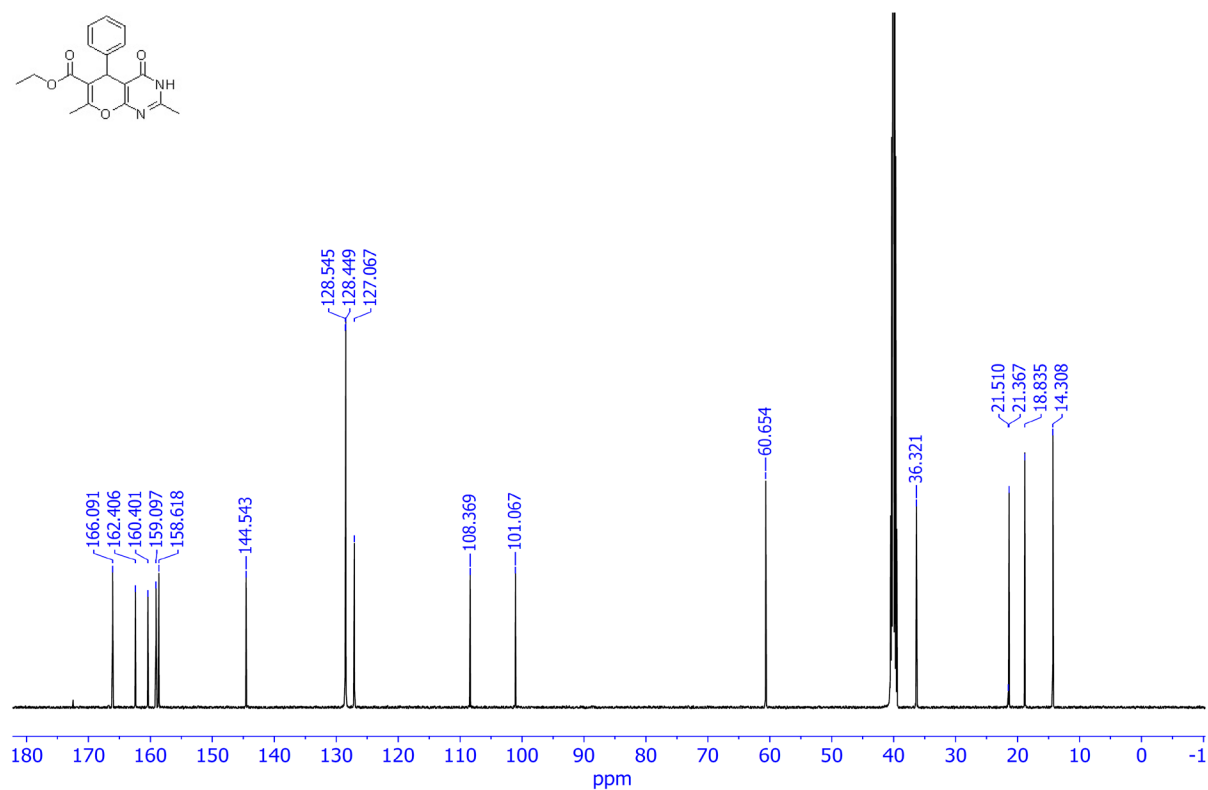
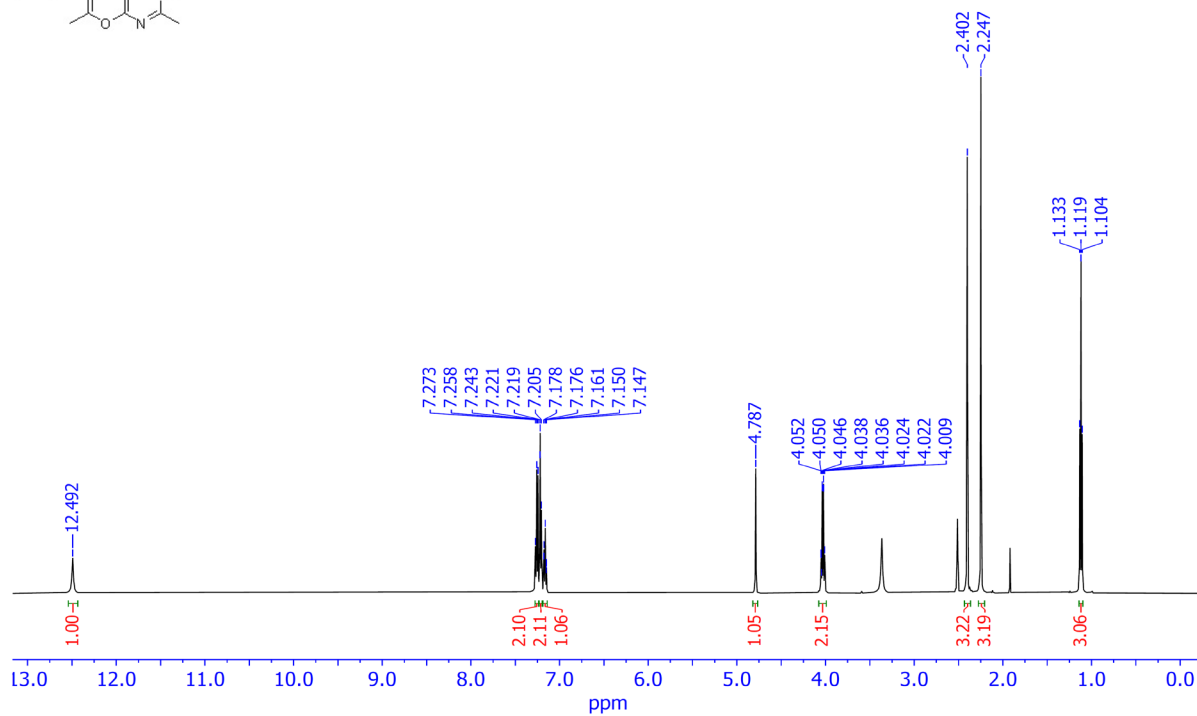
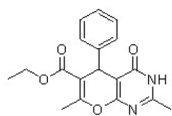
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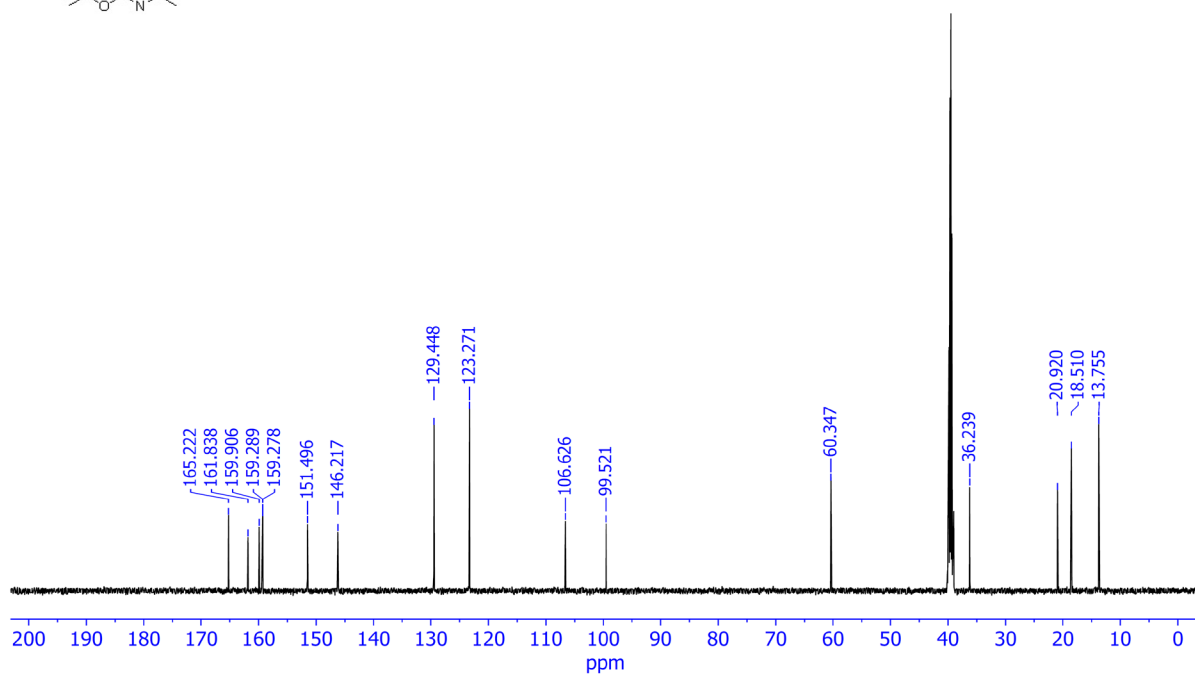
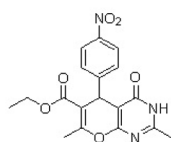
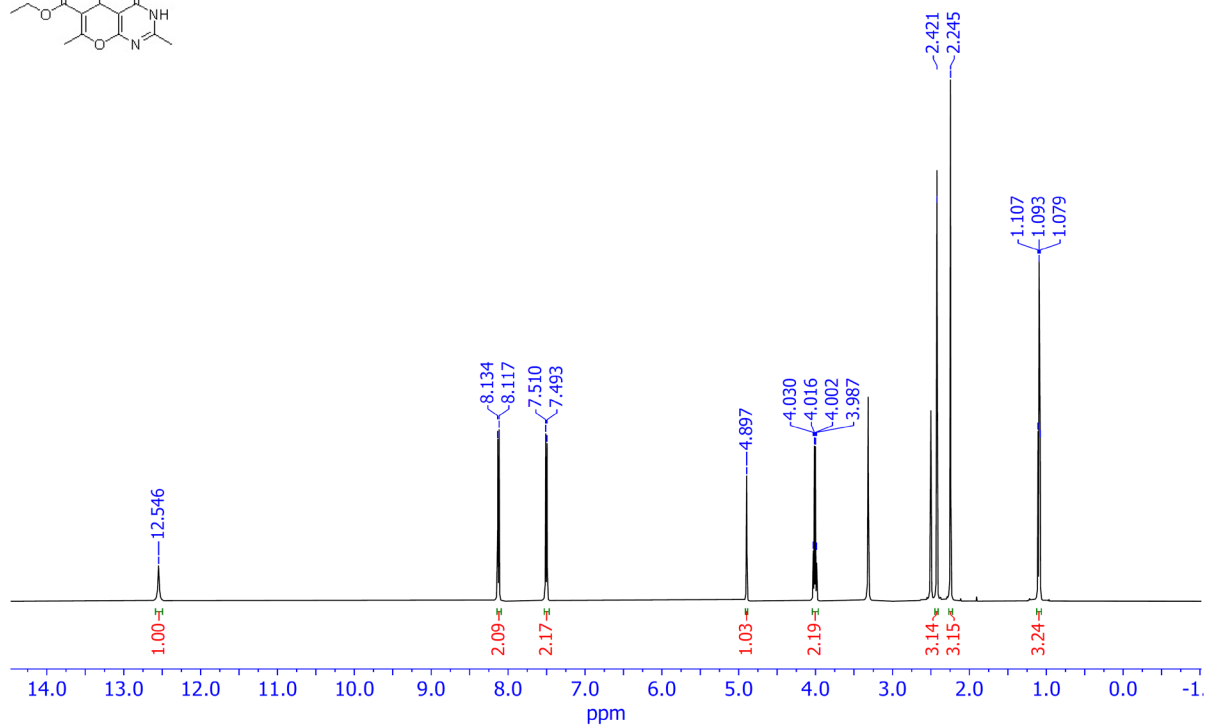
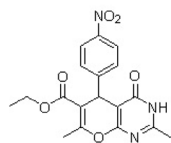
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#### 4. NMR spectra of compounds 5a-5s

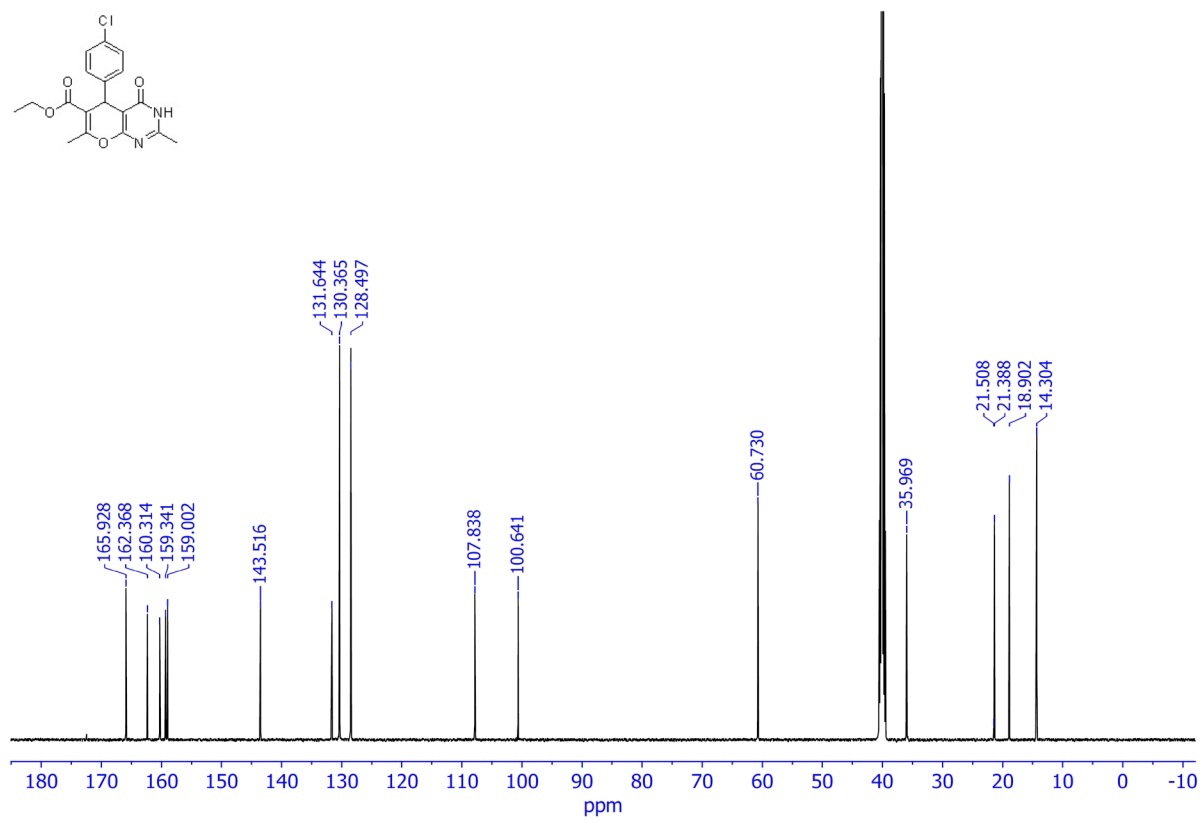
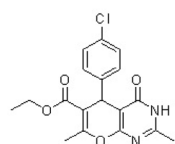
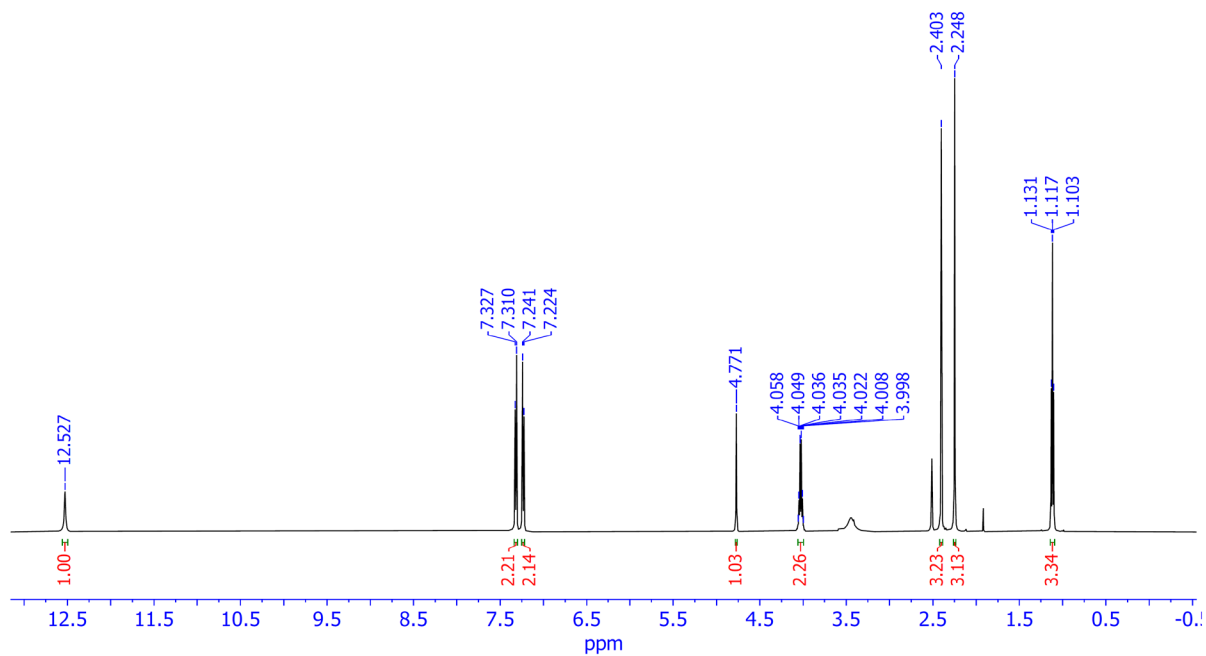
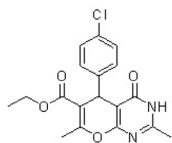
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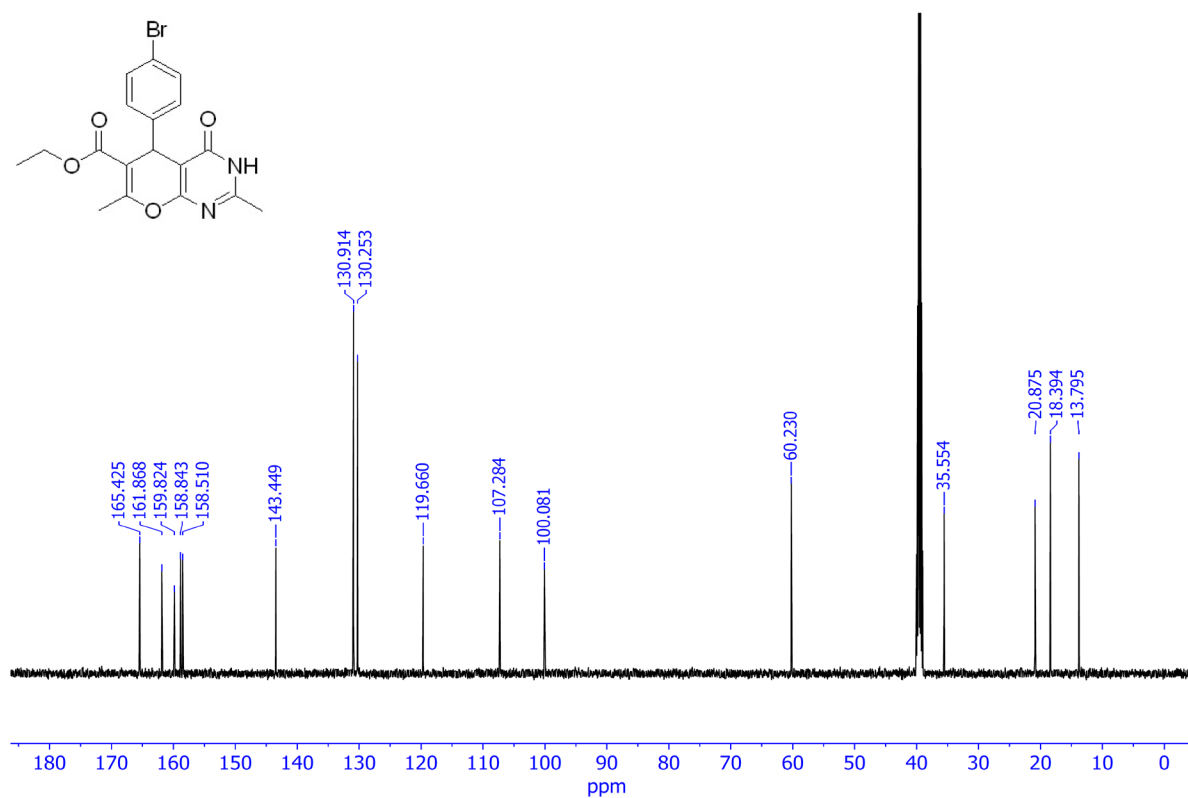
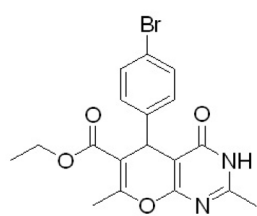
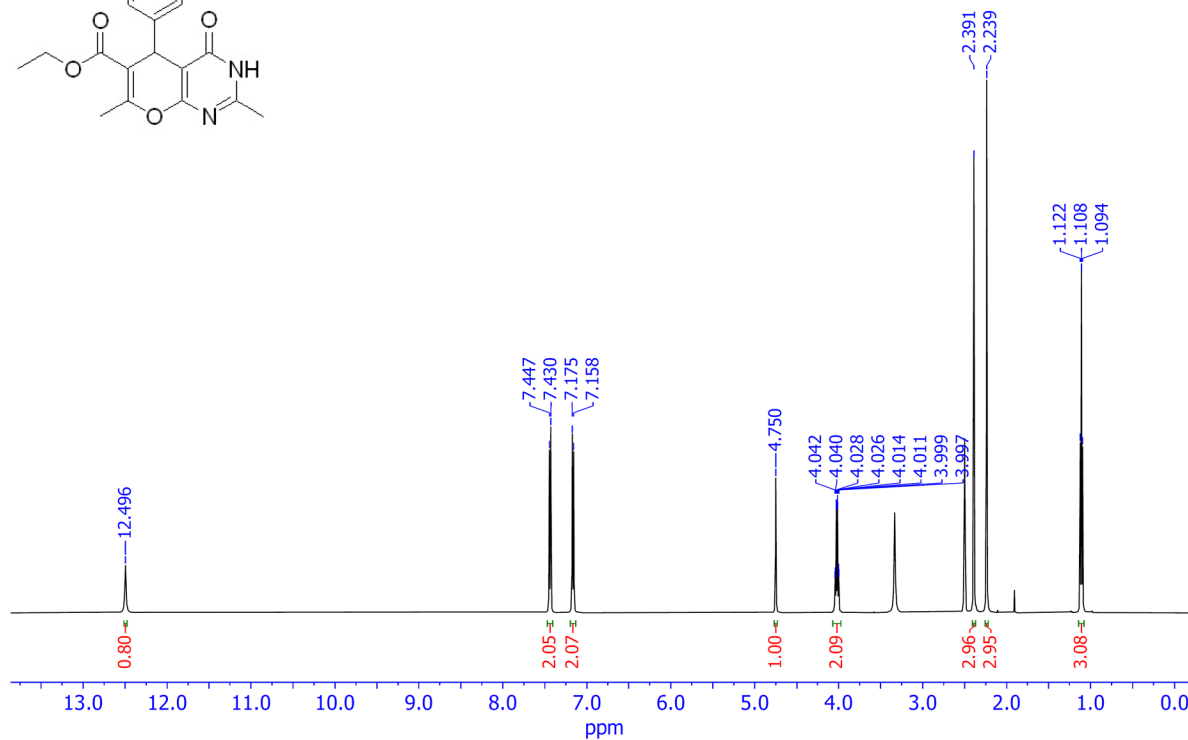
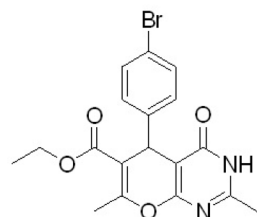
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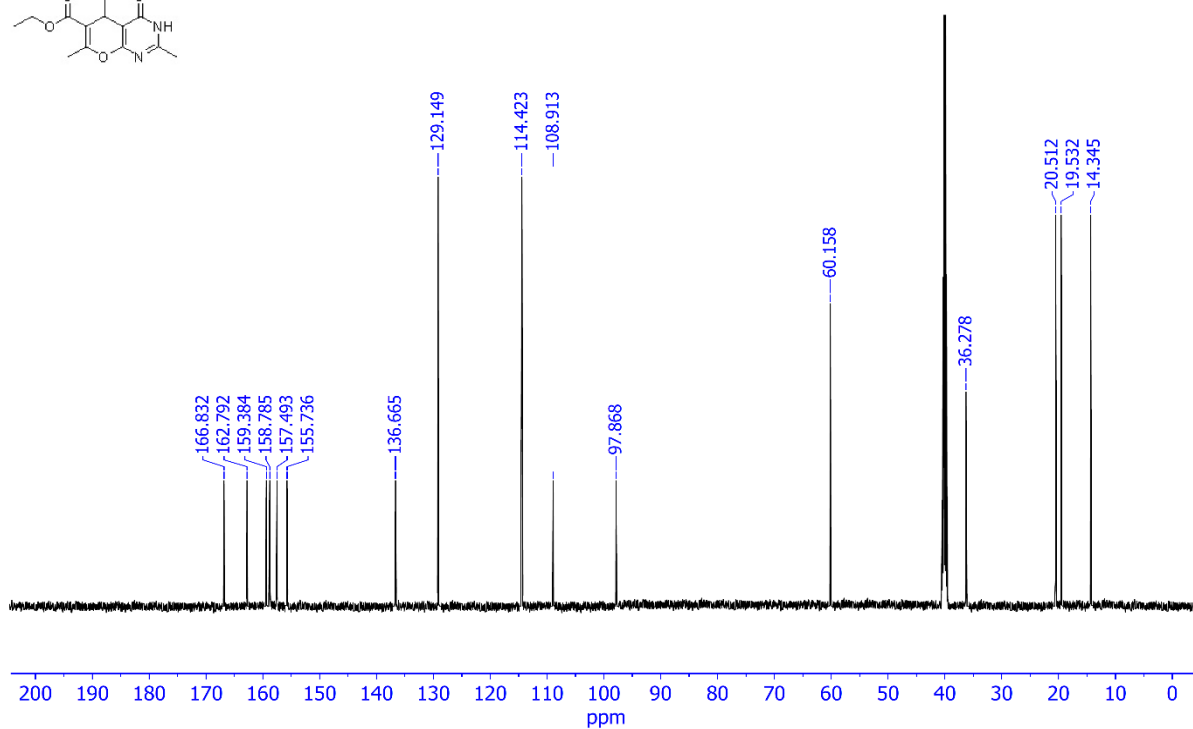
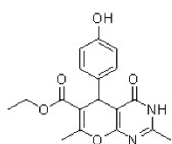
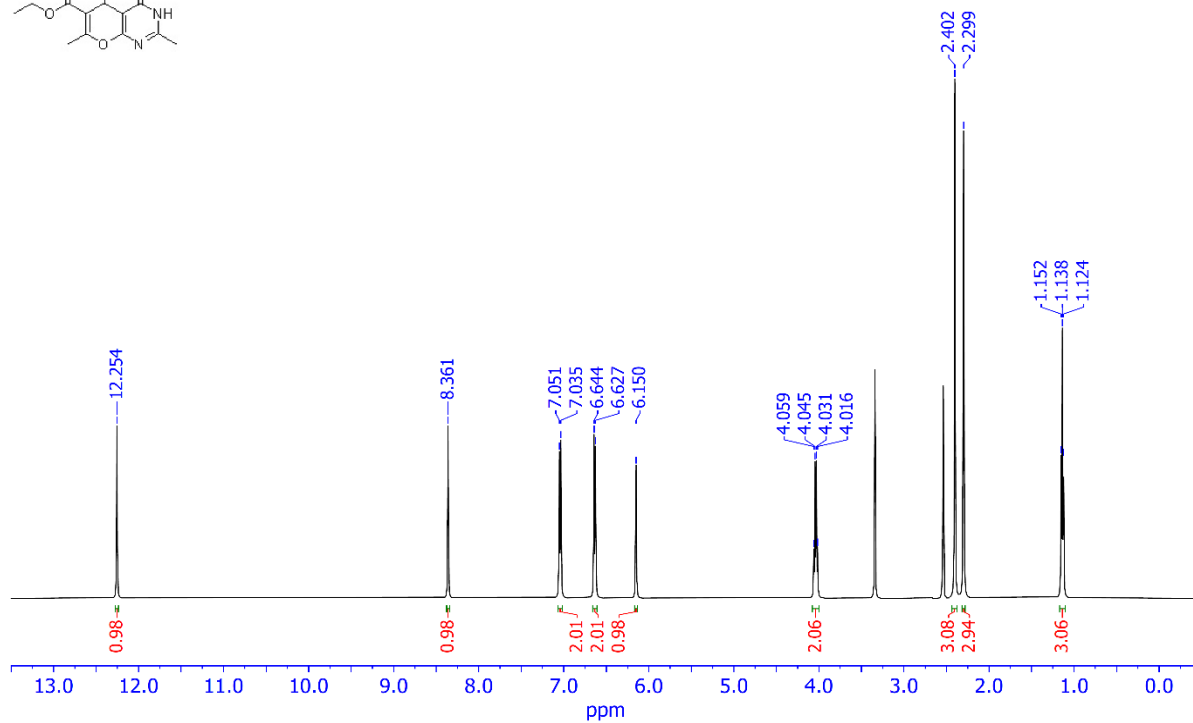
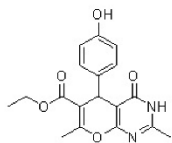
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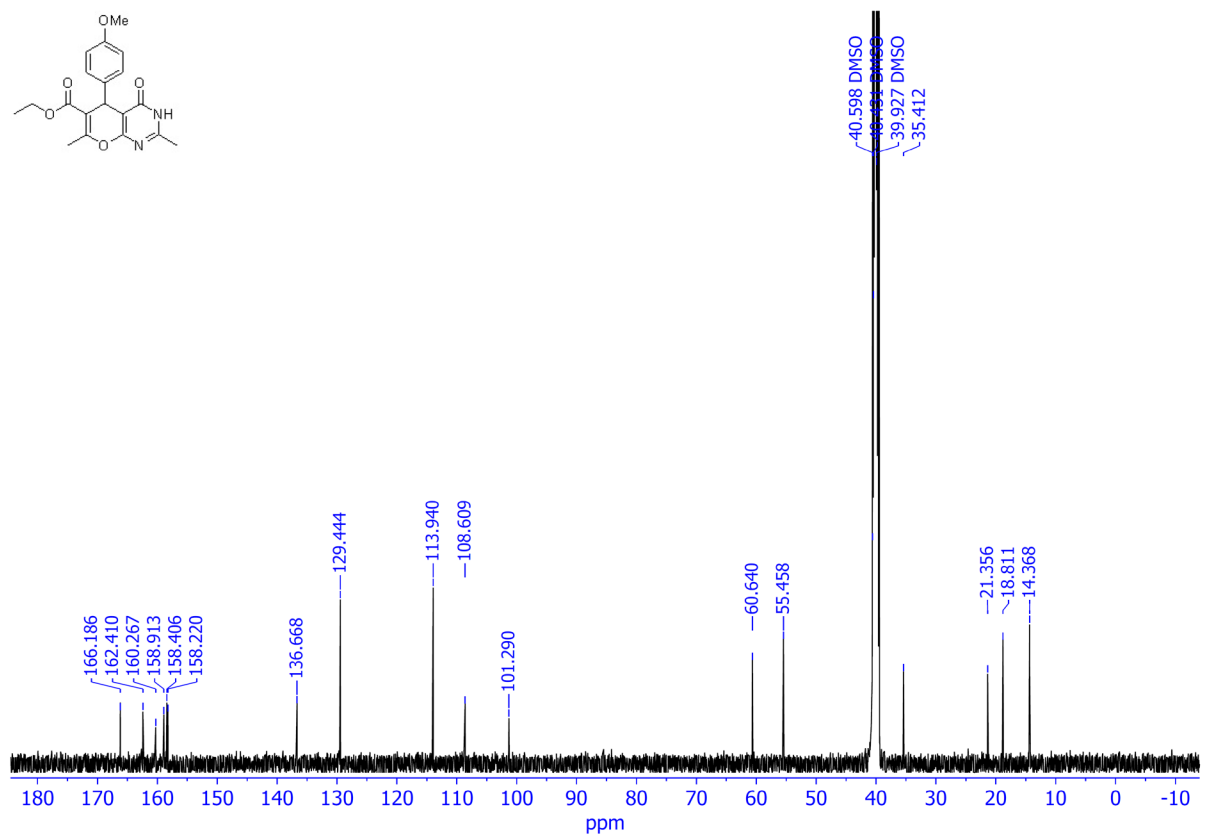
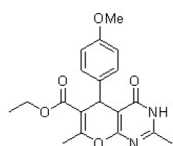
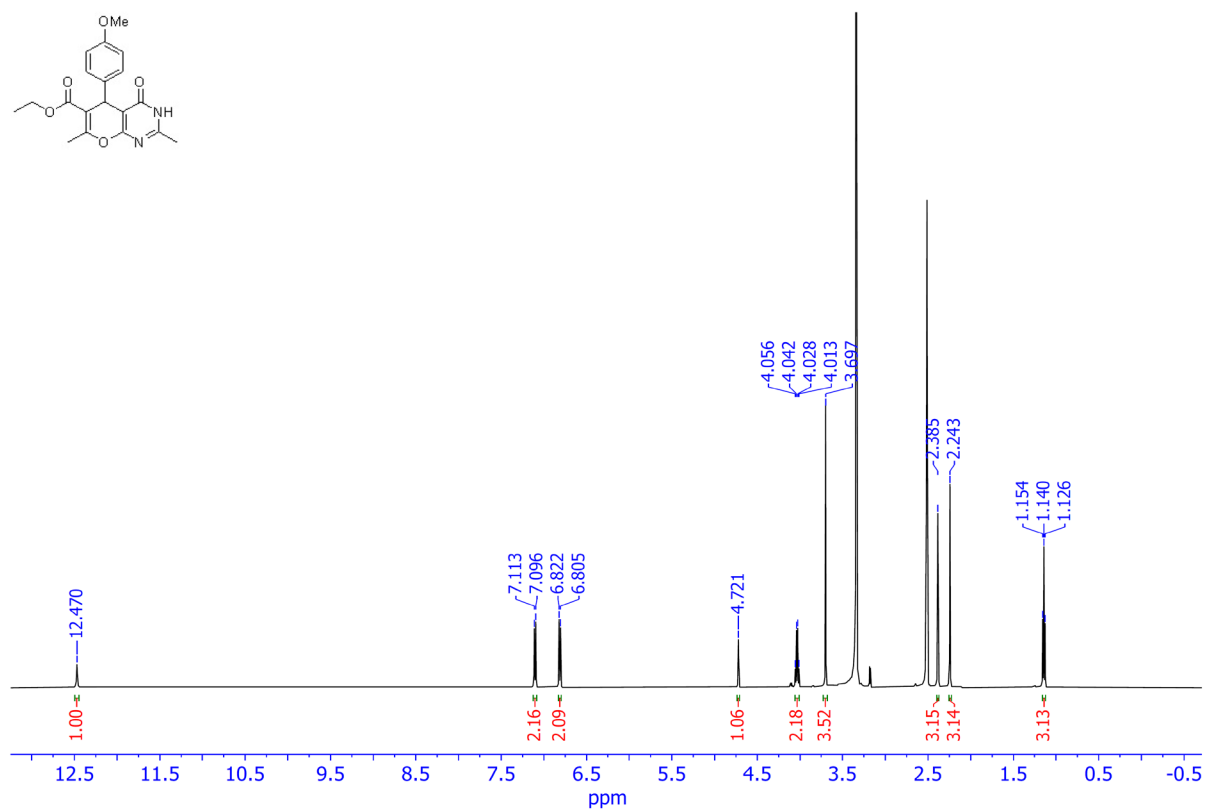
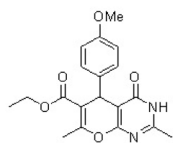
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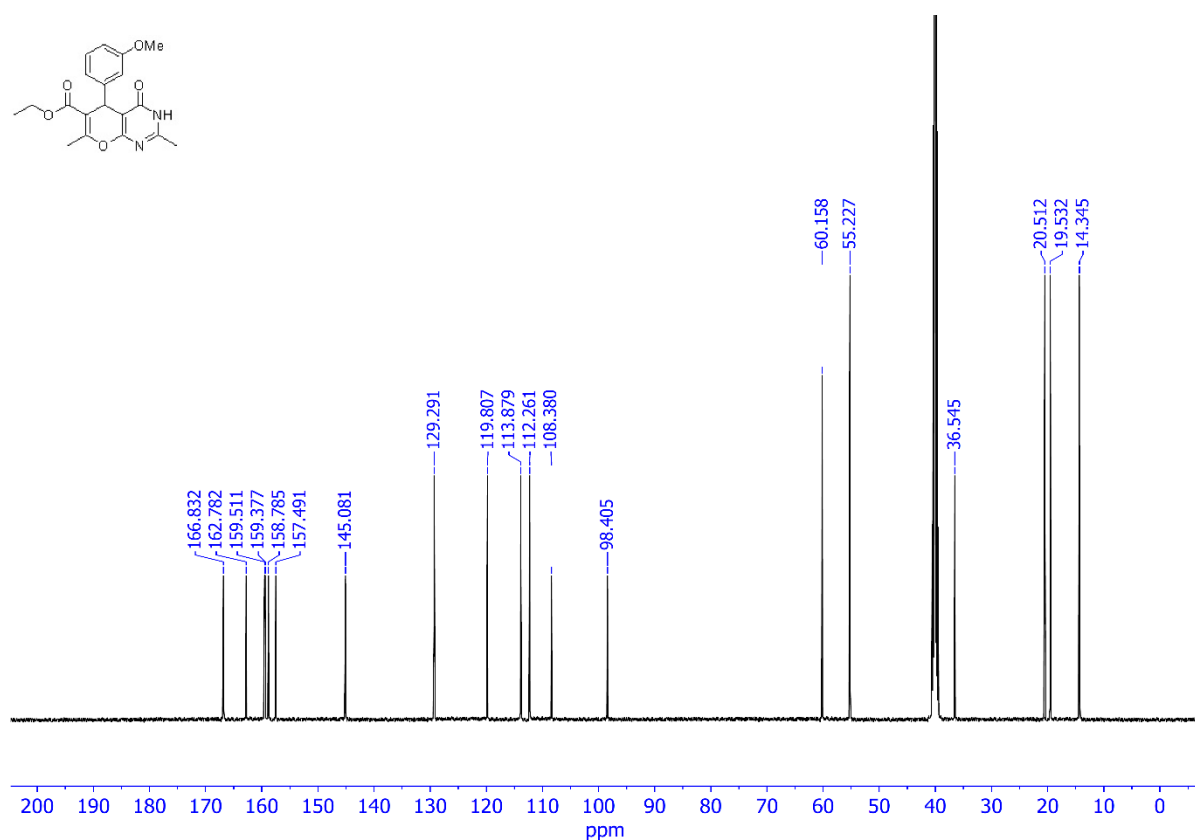
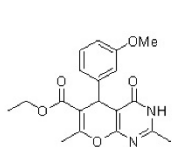
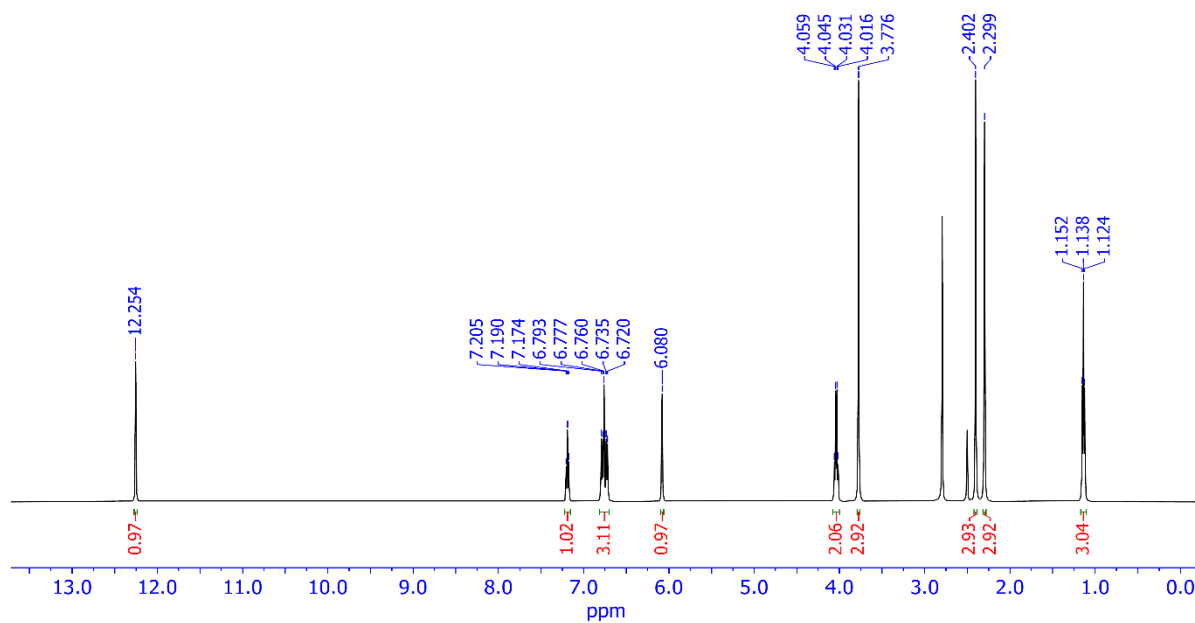
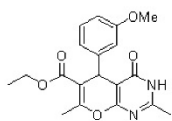
Ethyl 2,7-dimethyl-5-(4-hydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (**5i**)



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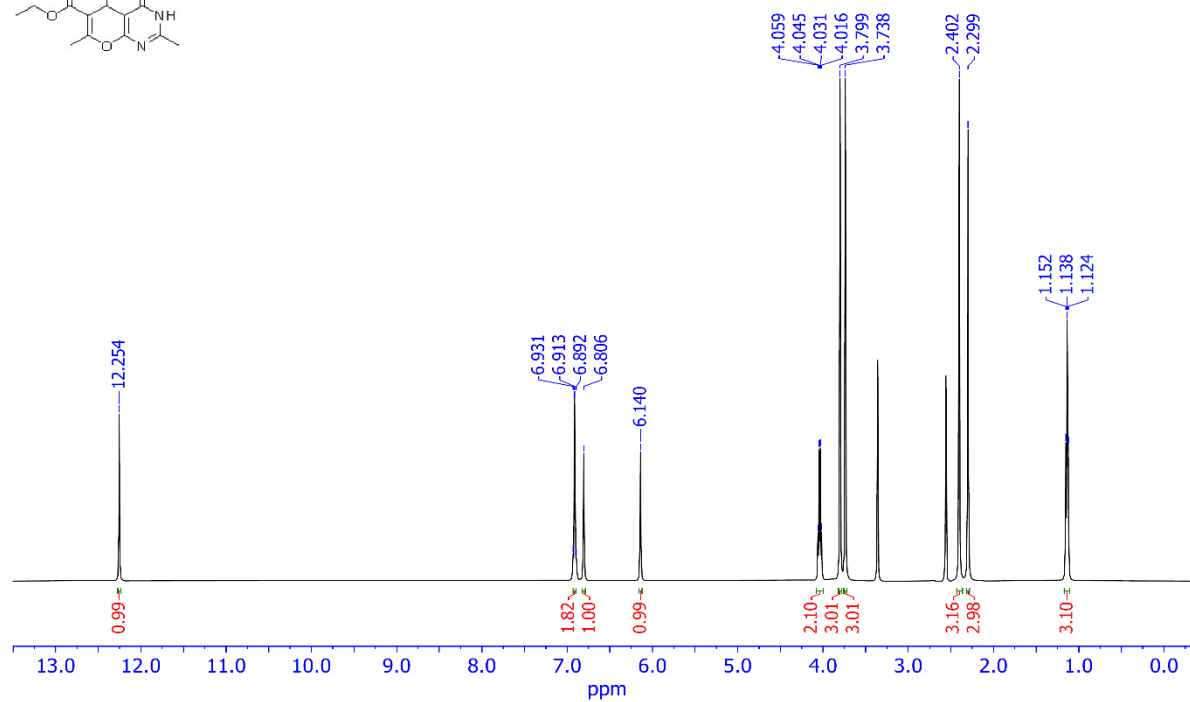
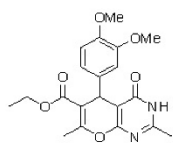


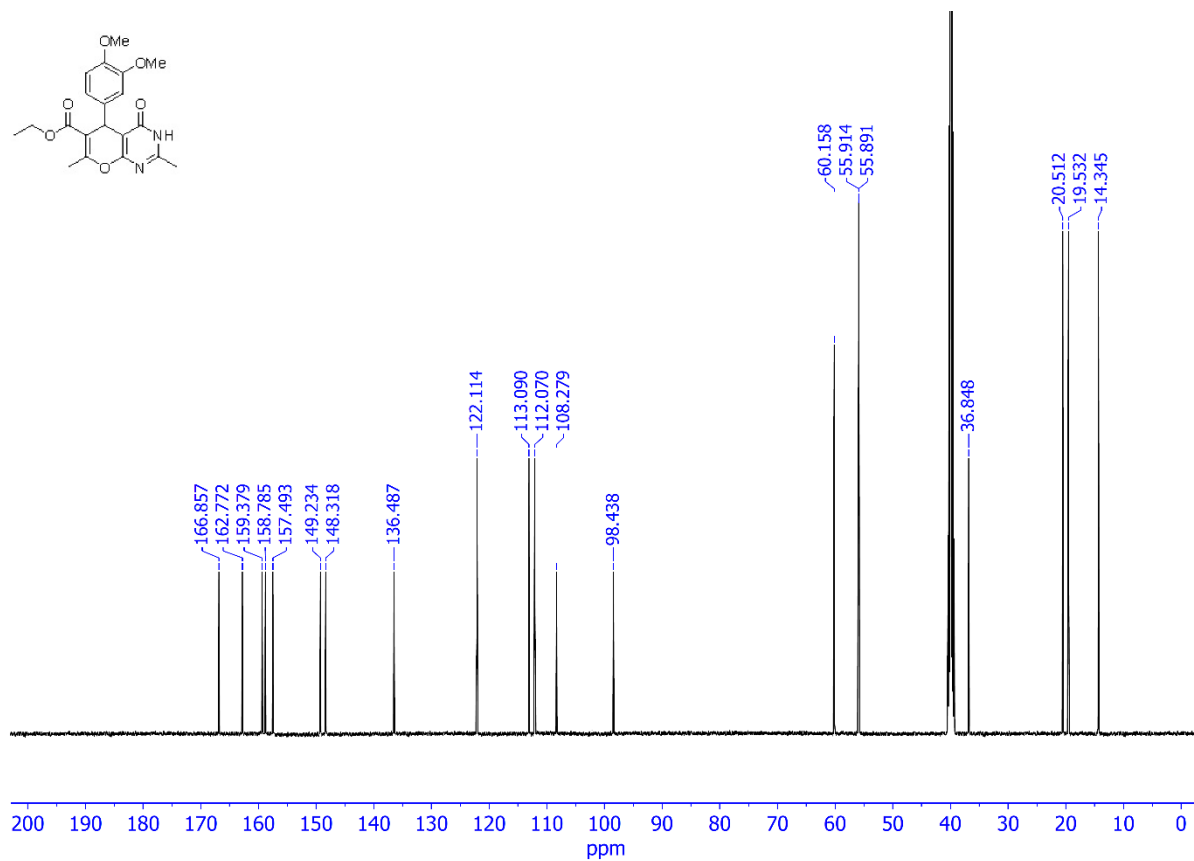
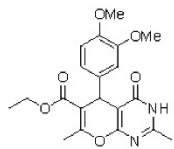
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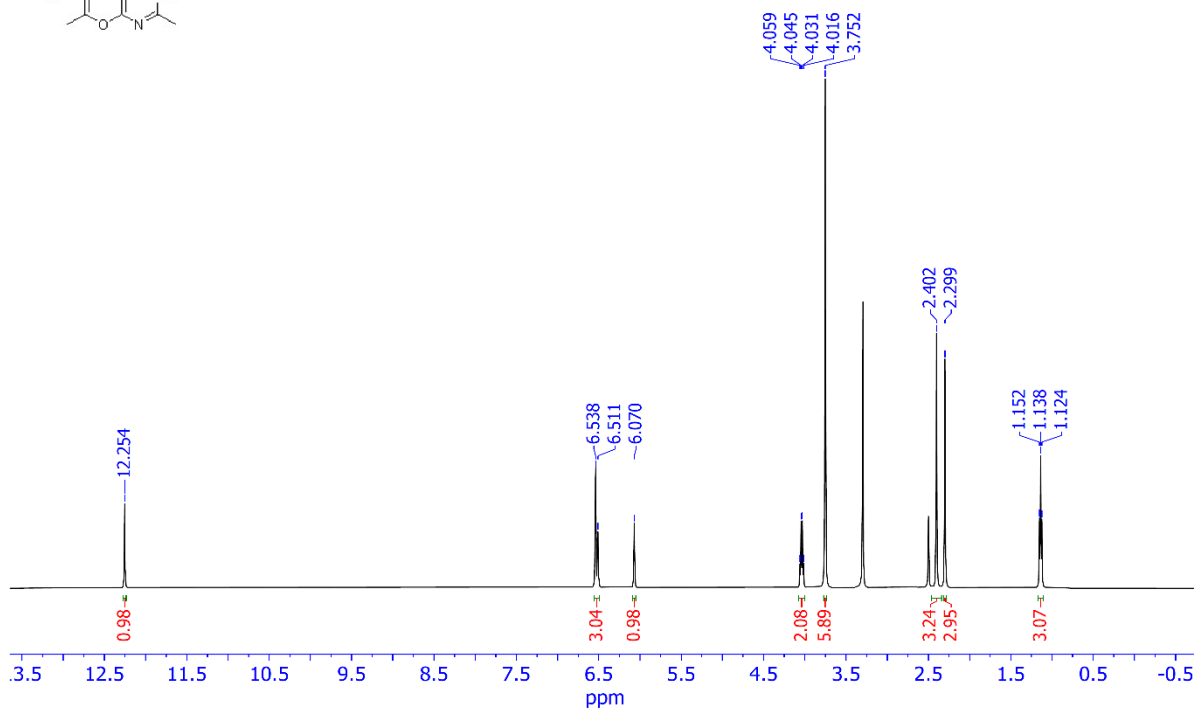
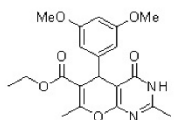


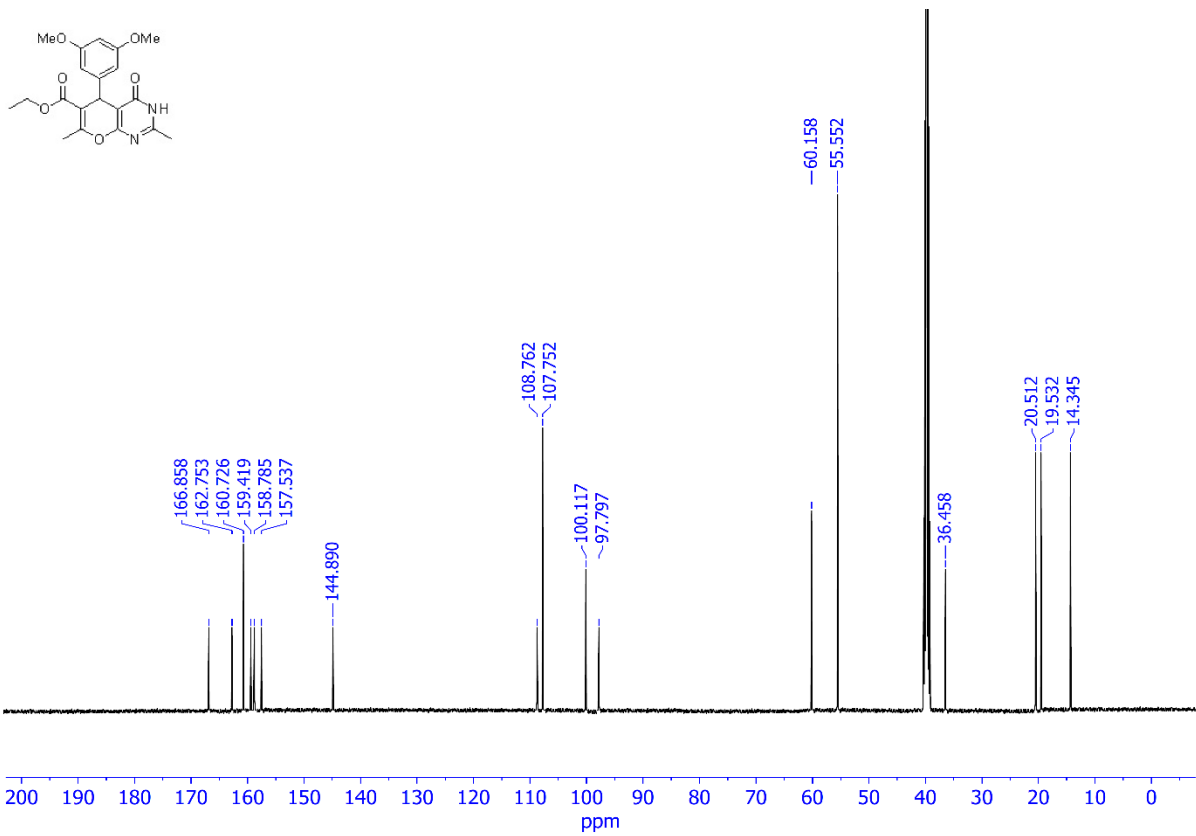
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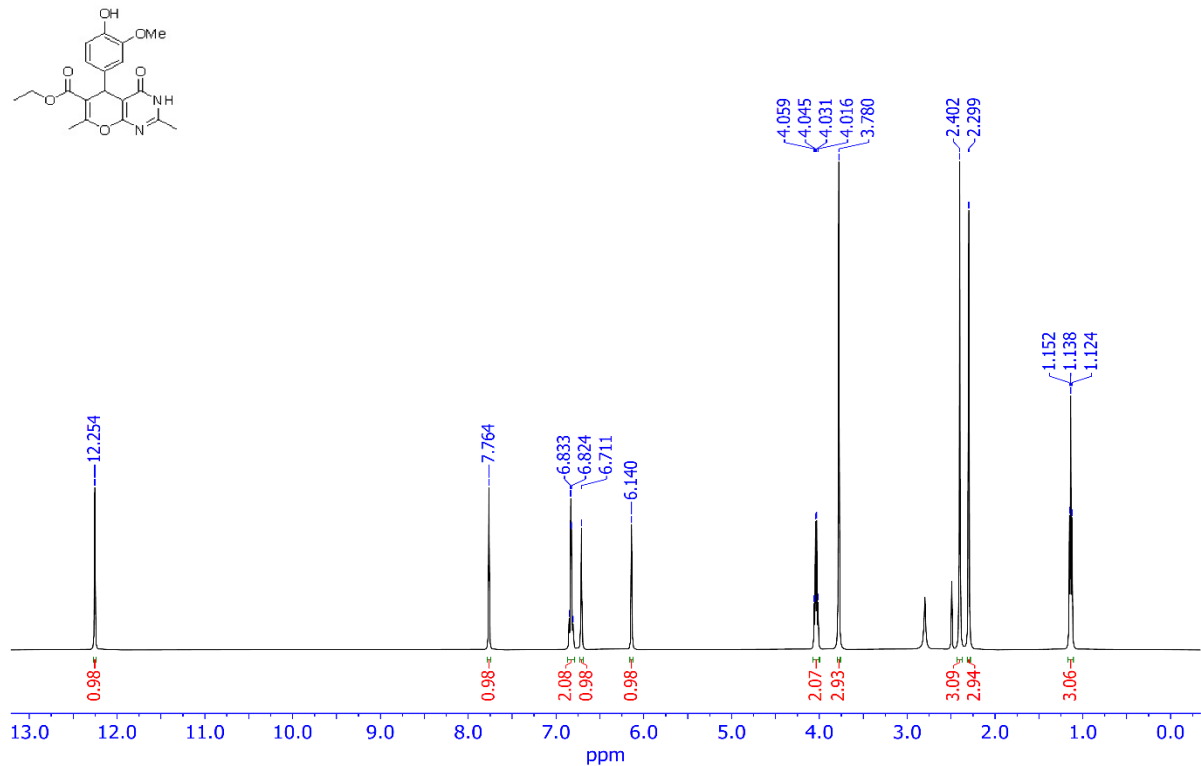


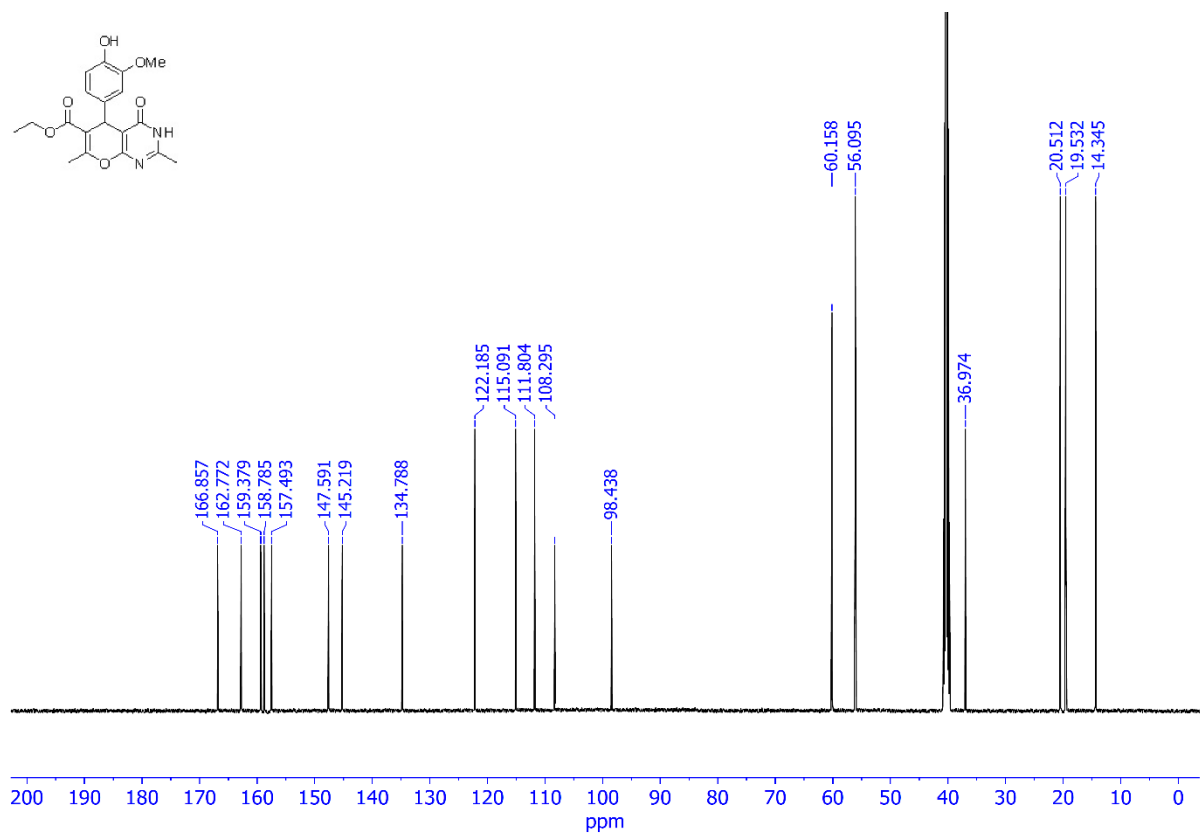
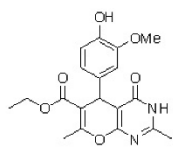
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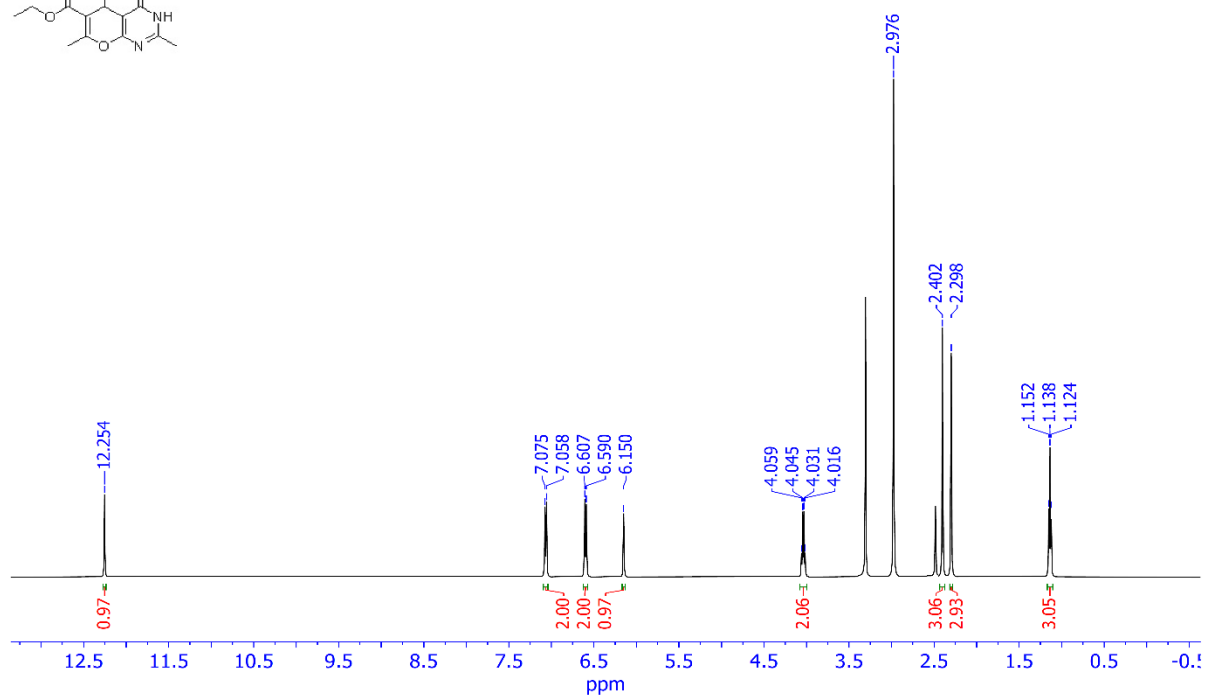
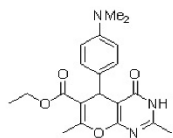


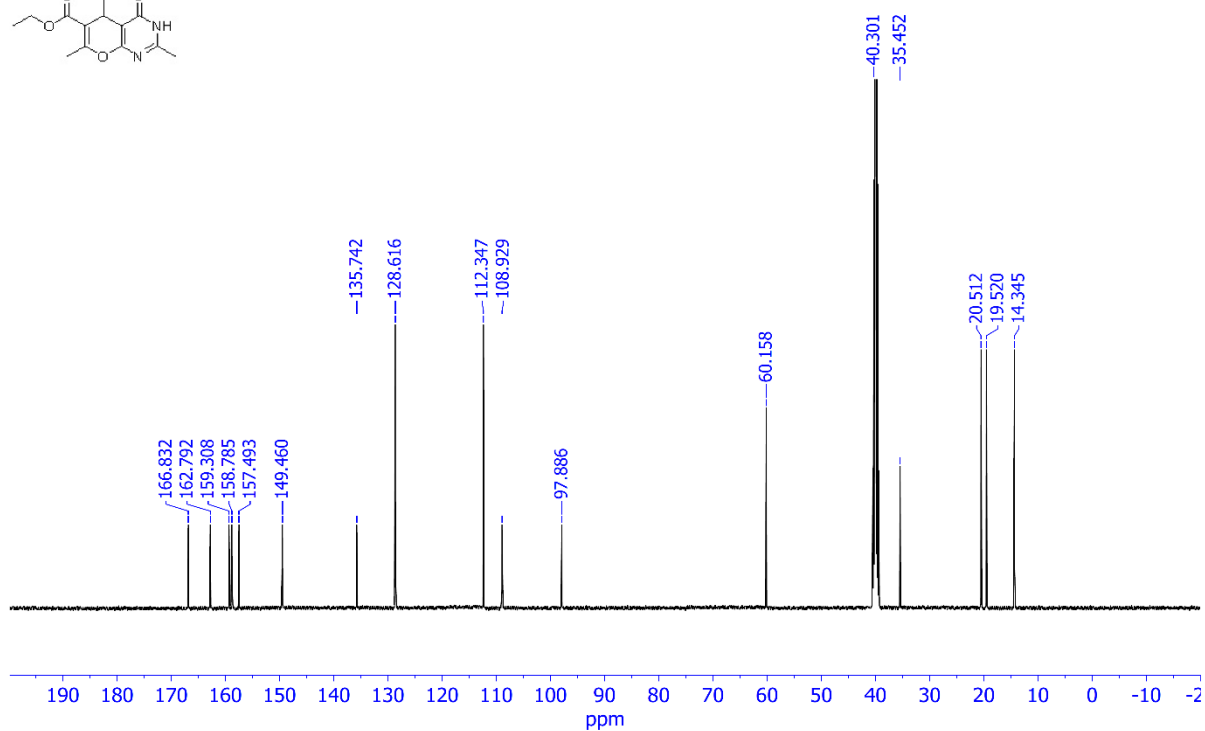
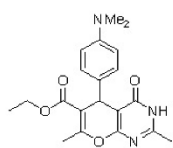
*Ethyl 2,7-dimethyl-5-(4-hydroxy-3-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (**50**)*





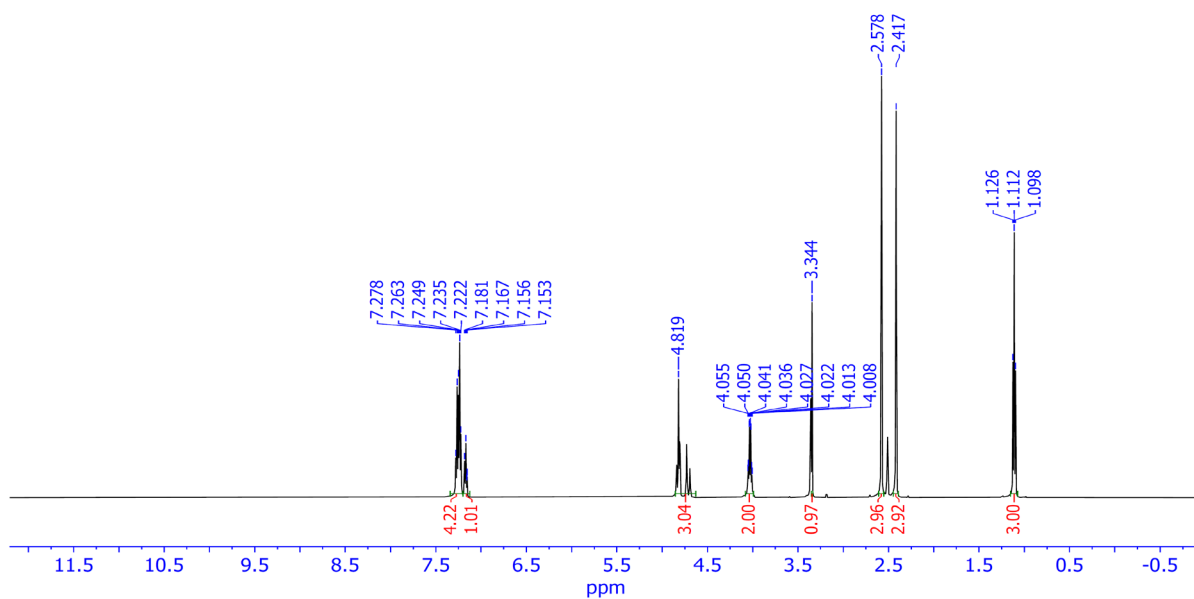
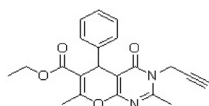
Ethyl 2,7-dimethyl-5-(4-dimethylaminophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (**5p**)

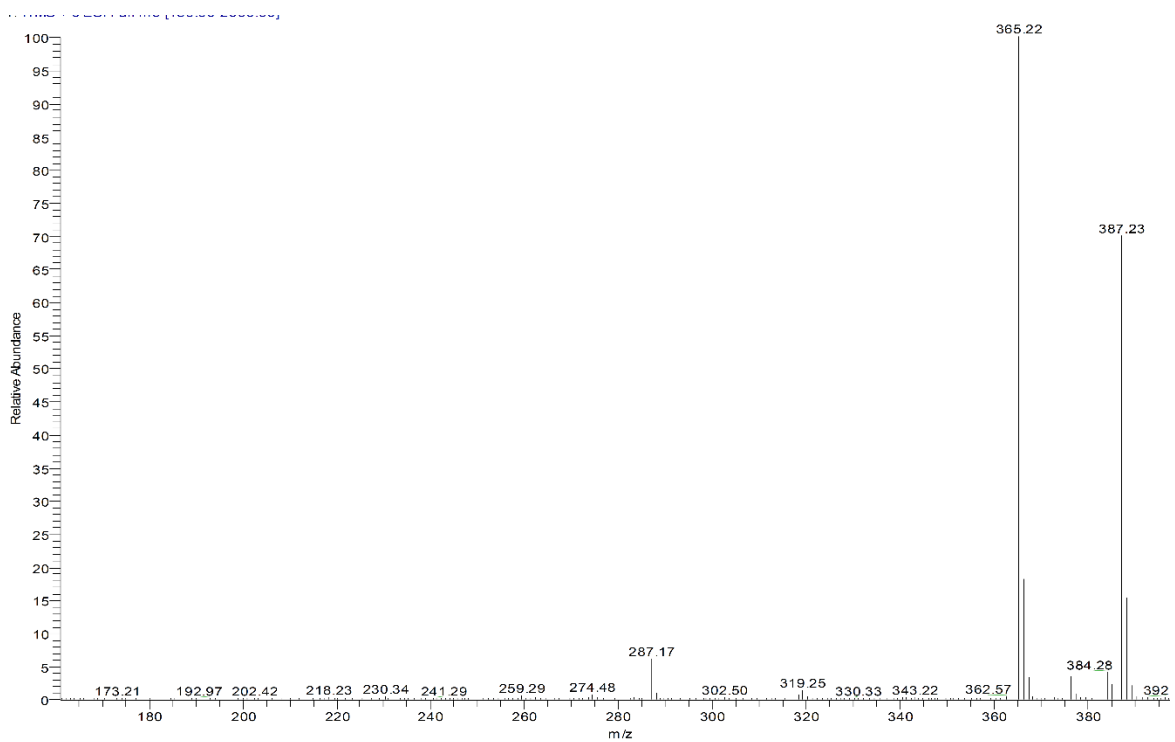
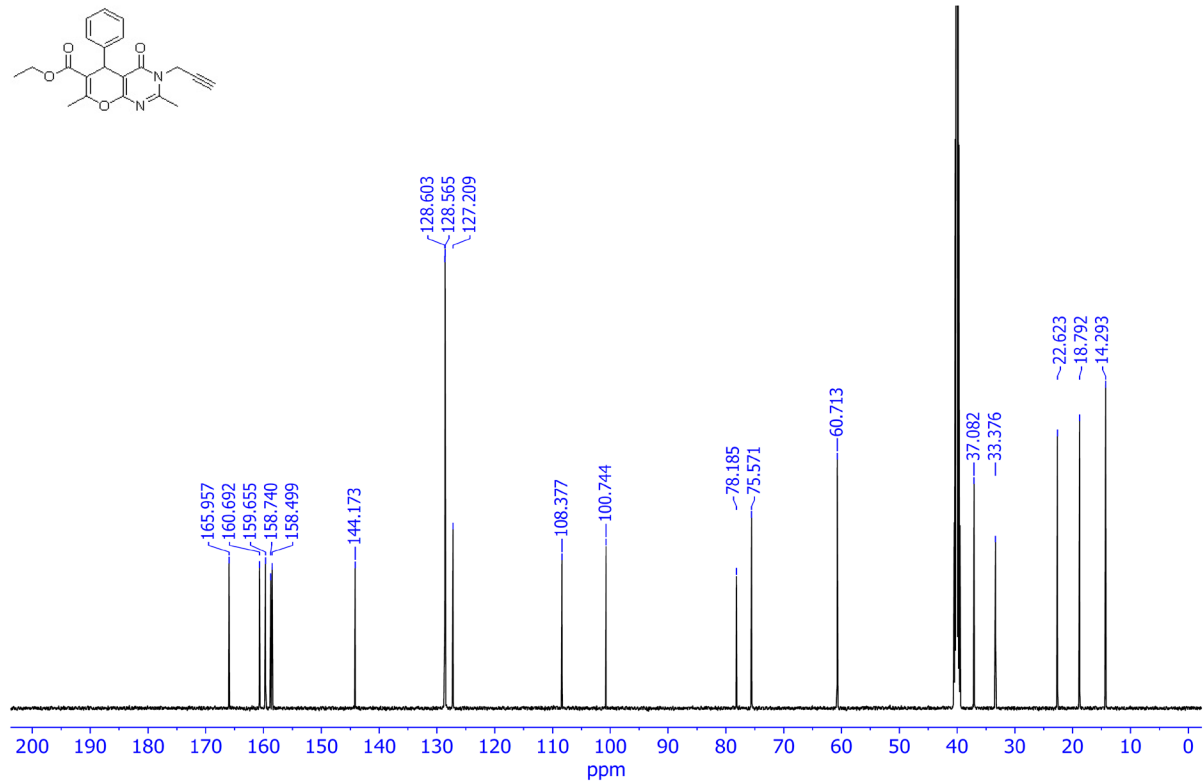
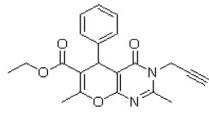




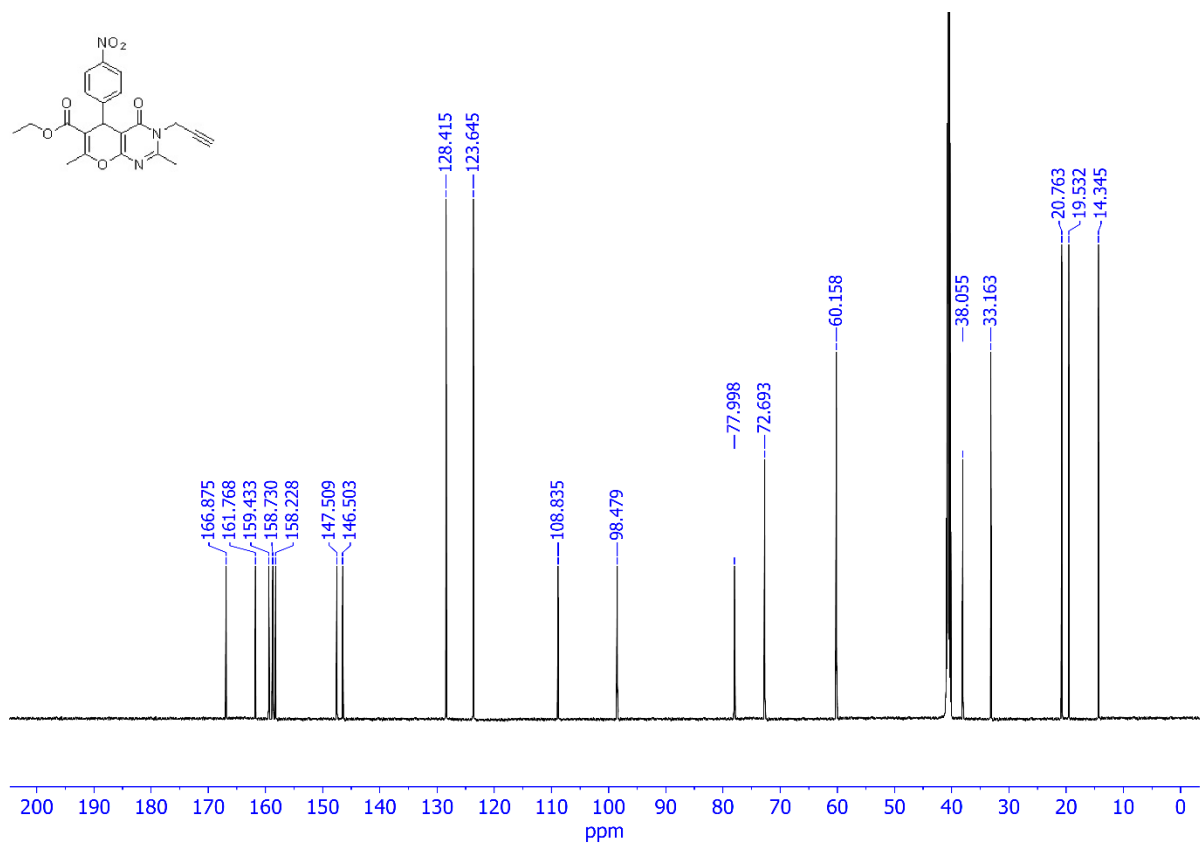
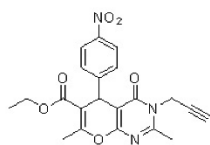
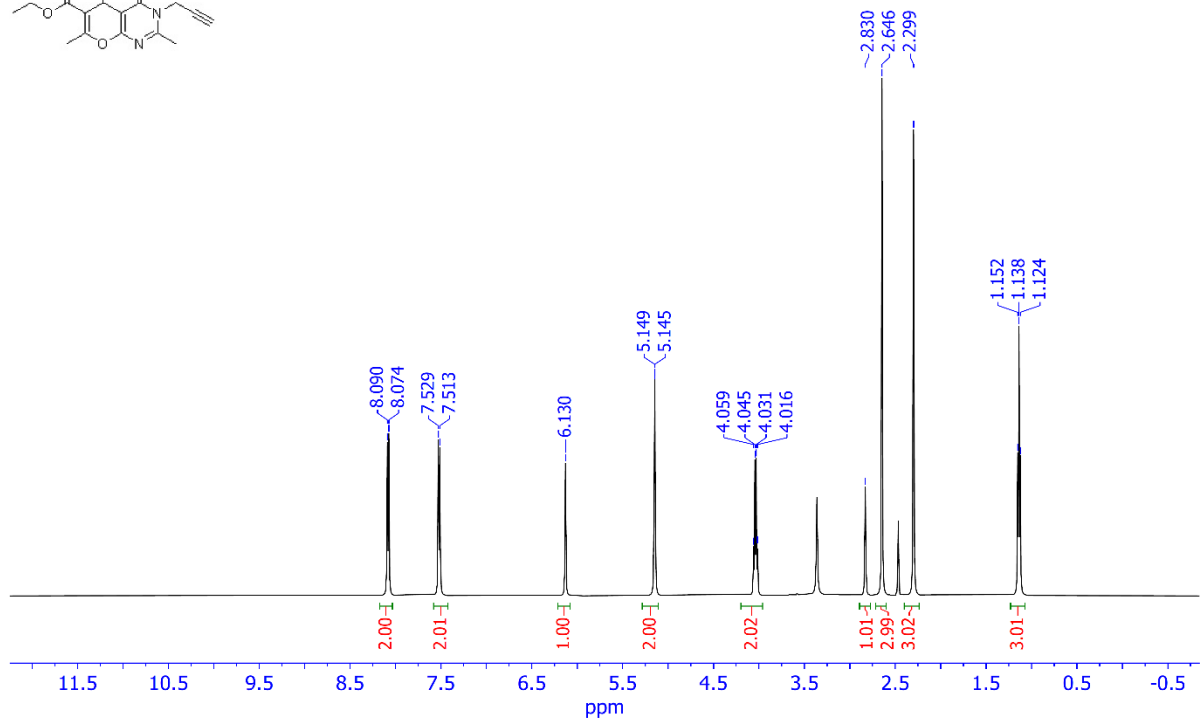
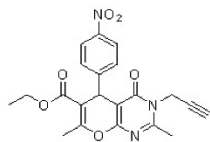
## 5. NMR and selected mass spectra of compounds 6a-6p

*Ethyl 2,7-dimethyl-5-phenyl-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6a)*

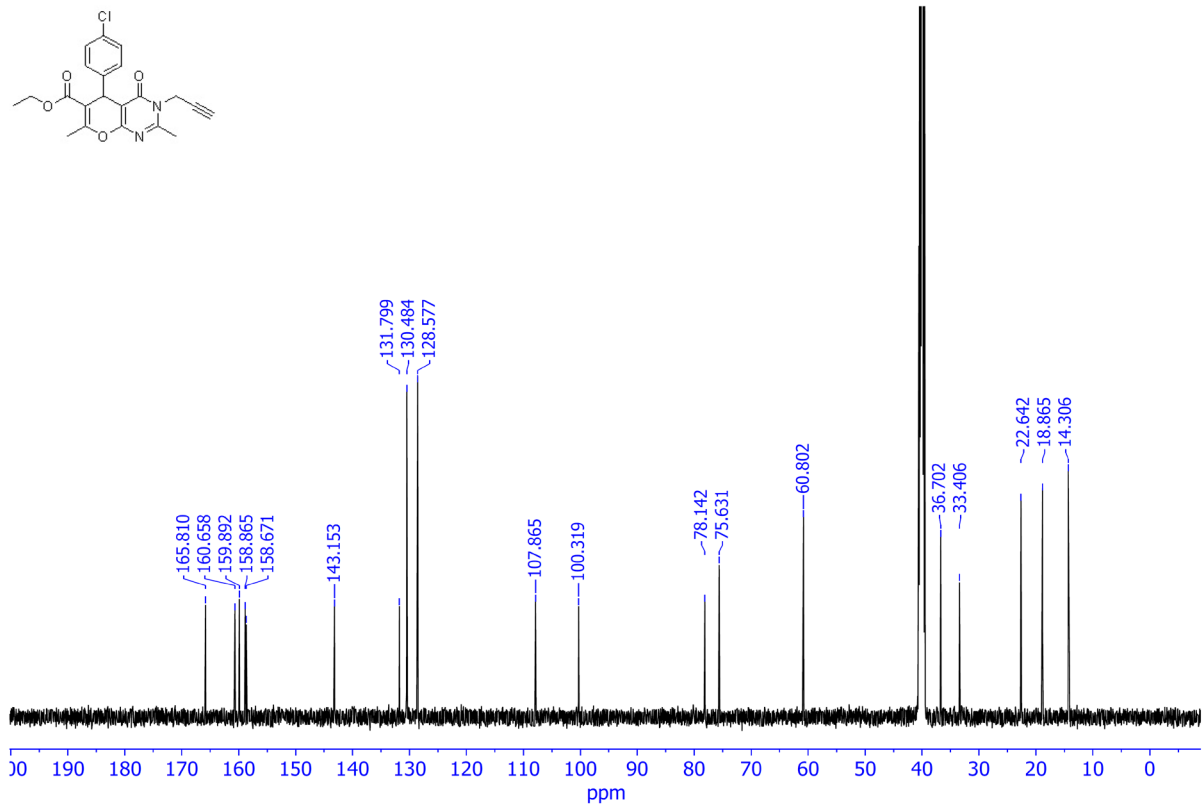
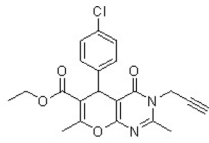
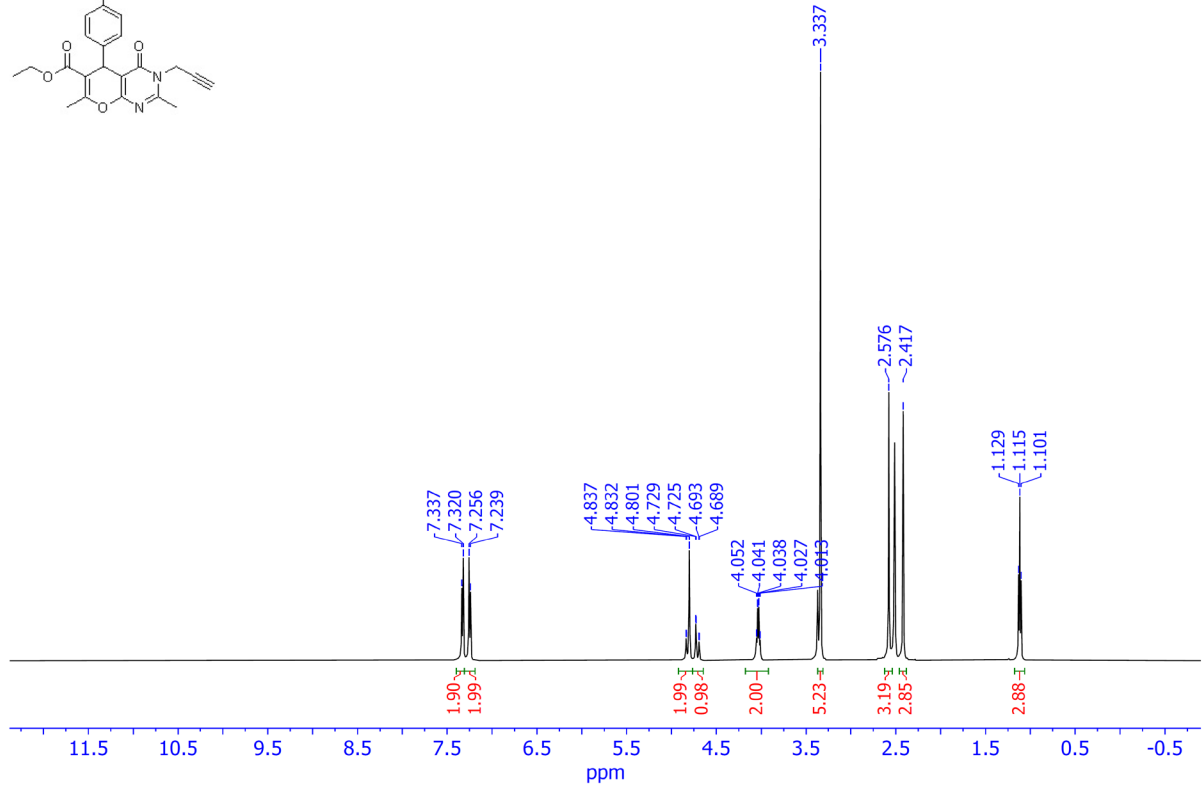
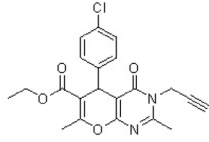




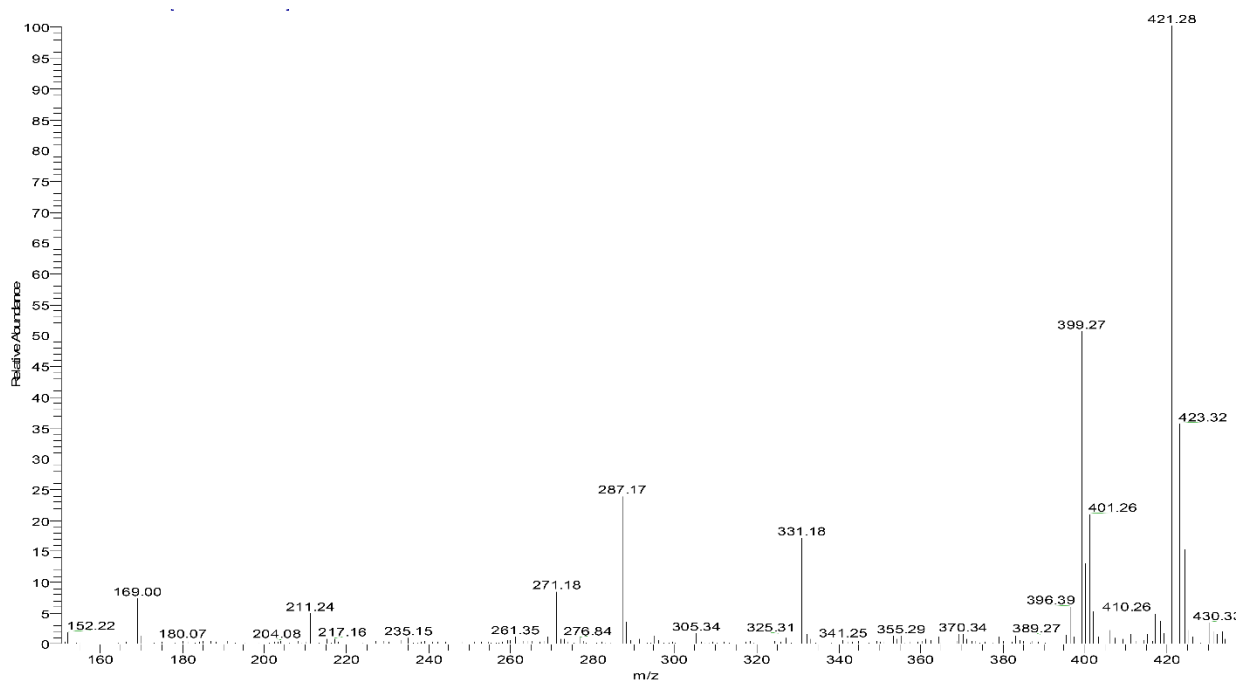
*Ethyl 2,7-dimethyl-5-(4-nitrophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6b)*



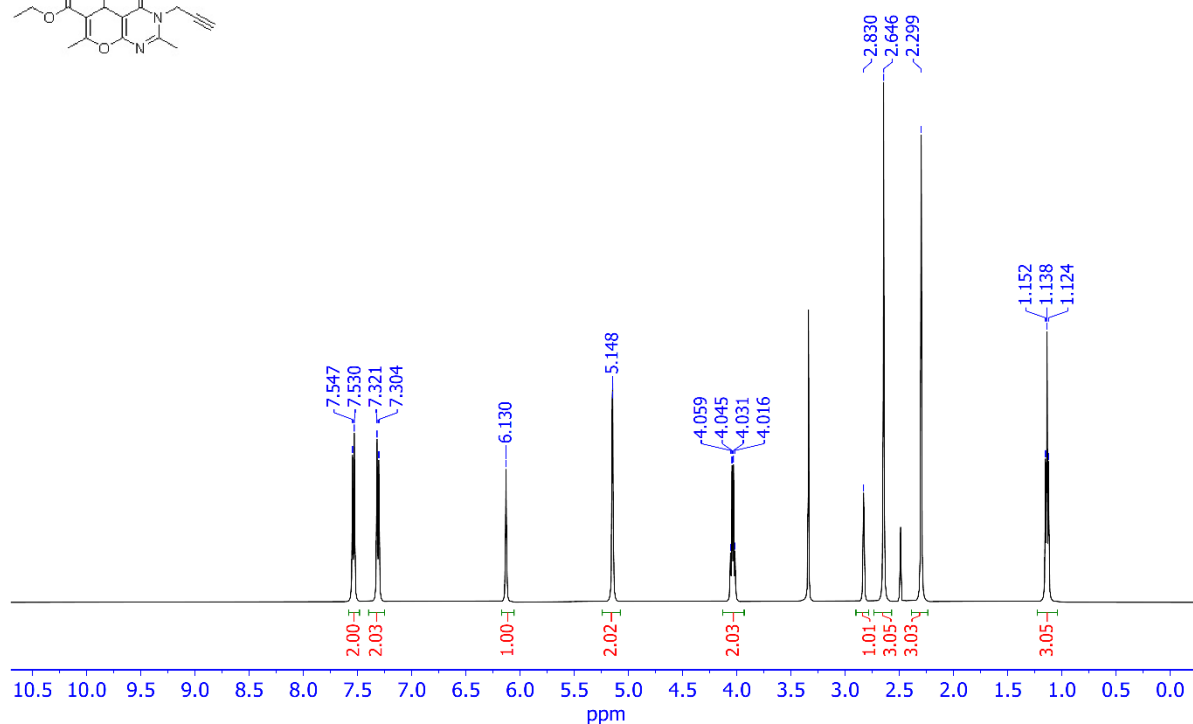
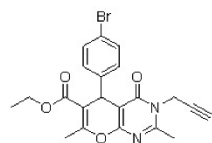
*Ethyl 2,7-dimethyl-5-(4-chlorophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6d)*

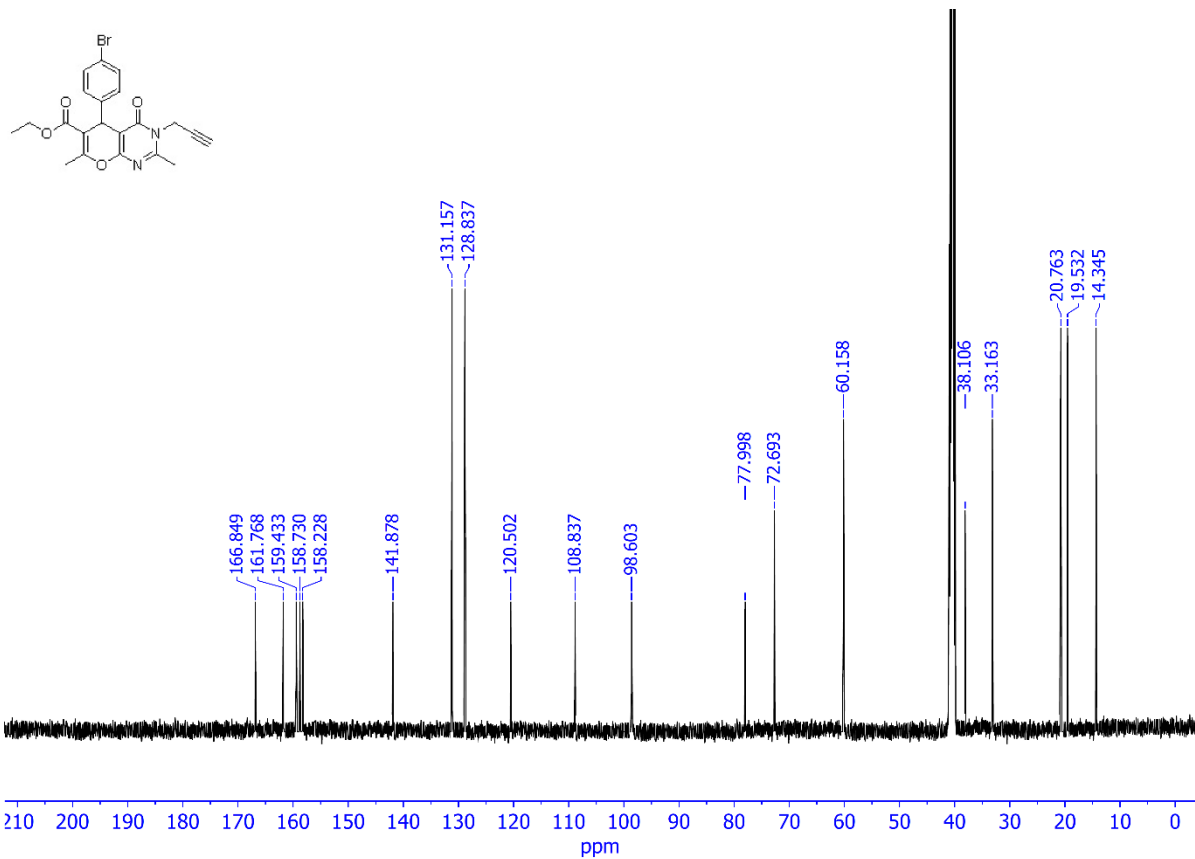




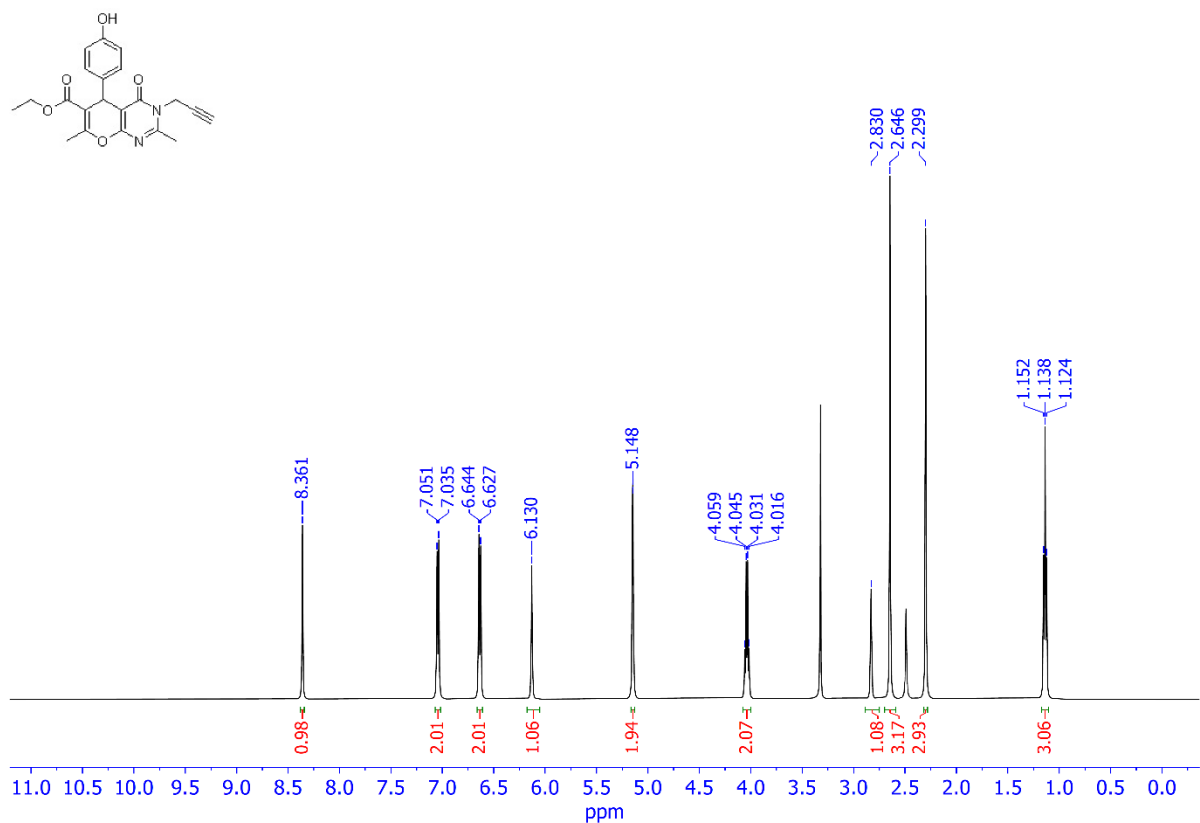


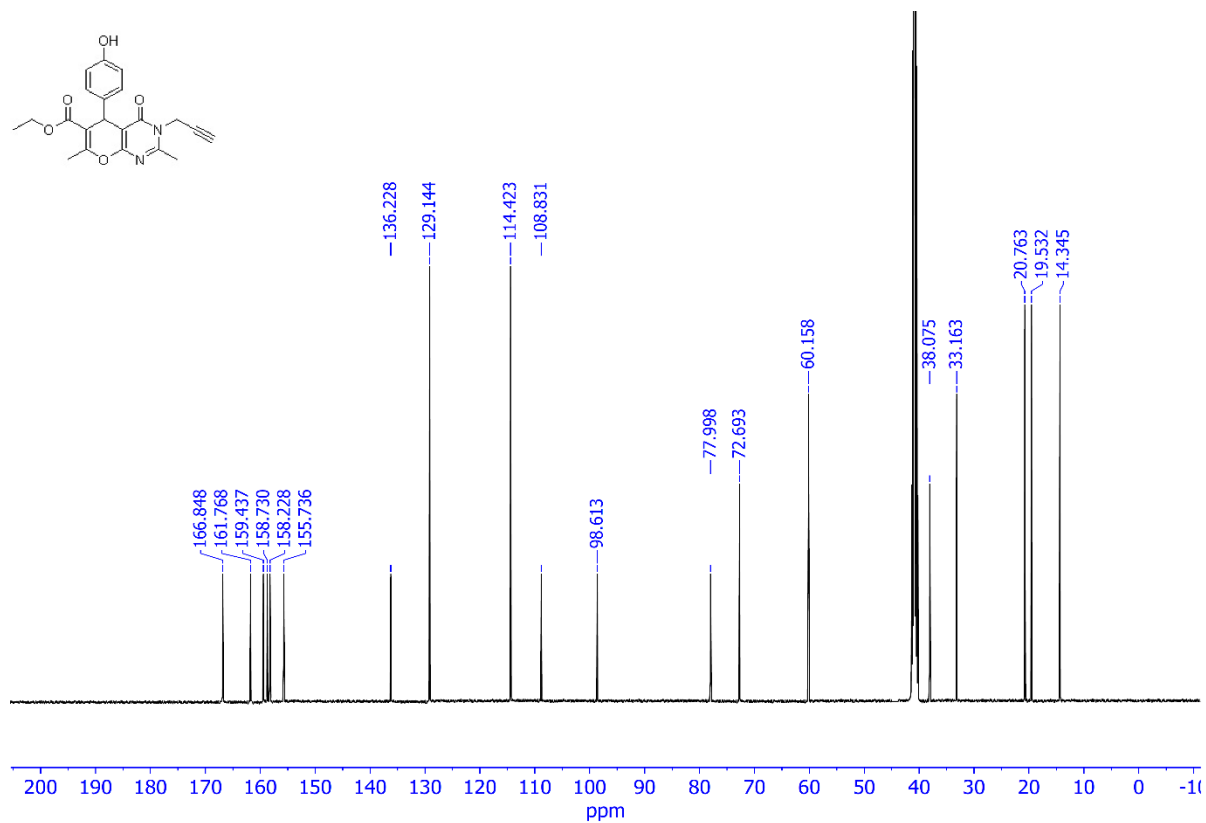
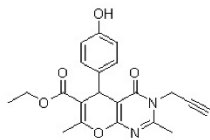
*Ethyl 2,7-dimethyl-5-(4-bromophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6f)*



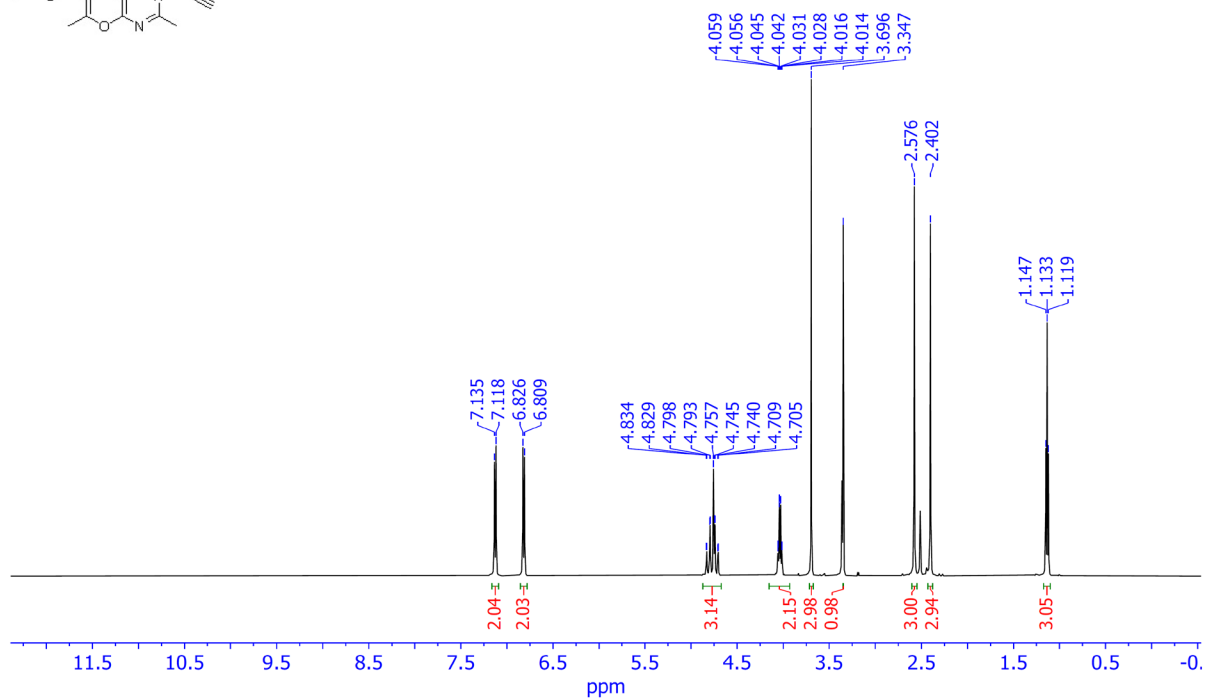
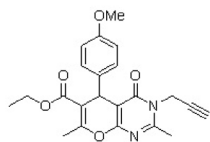


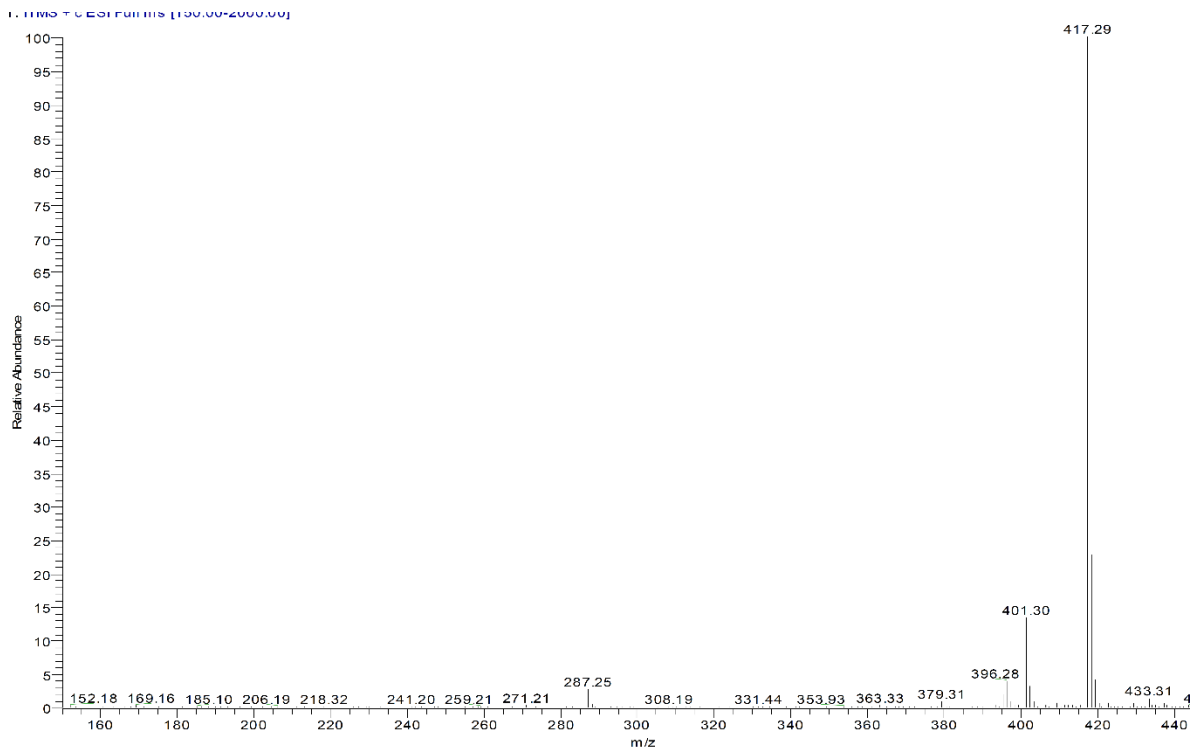
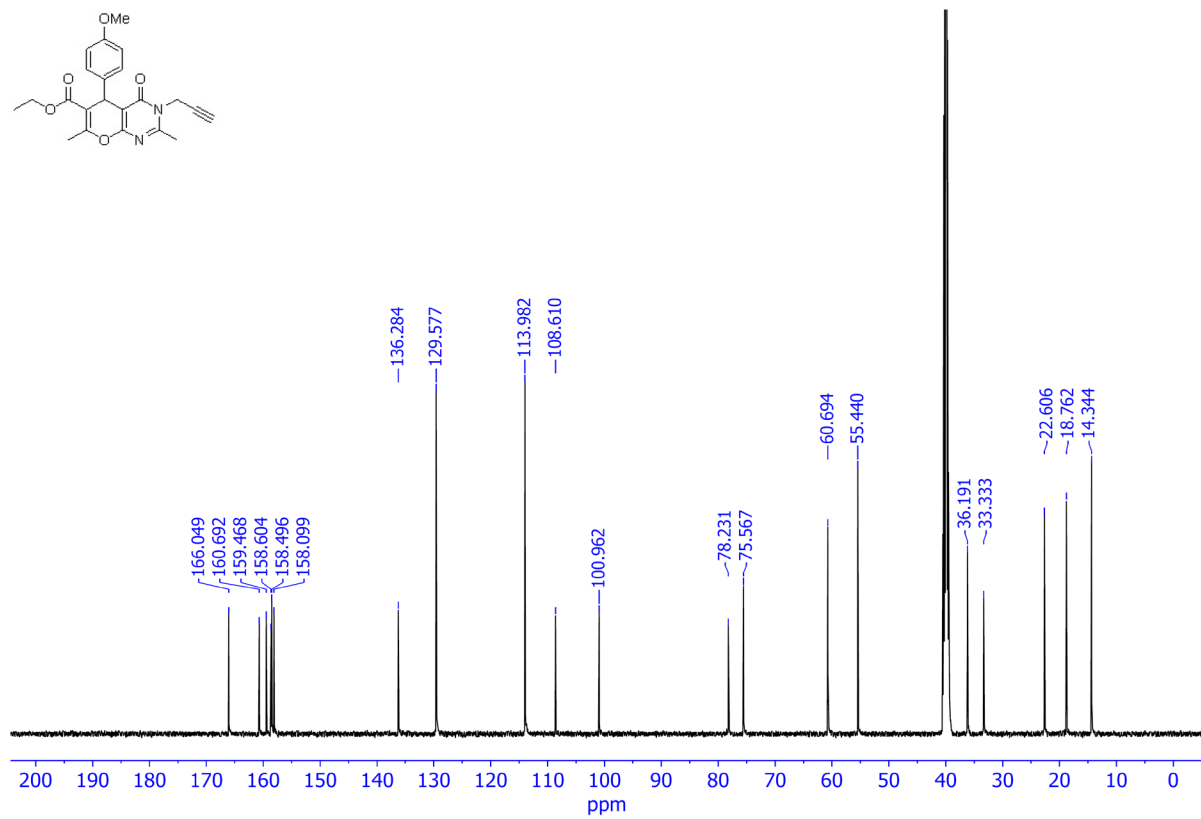
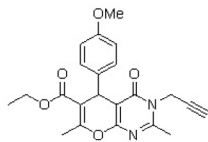
Ethyl 2,7-dimethyl-5-(4-hydroxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (**6i**)



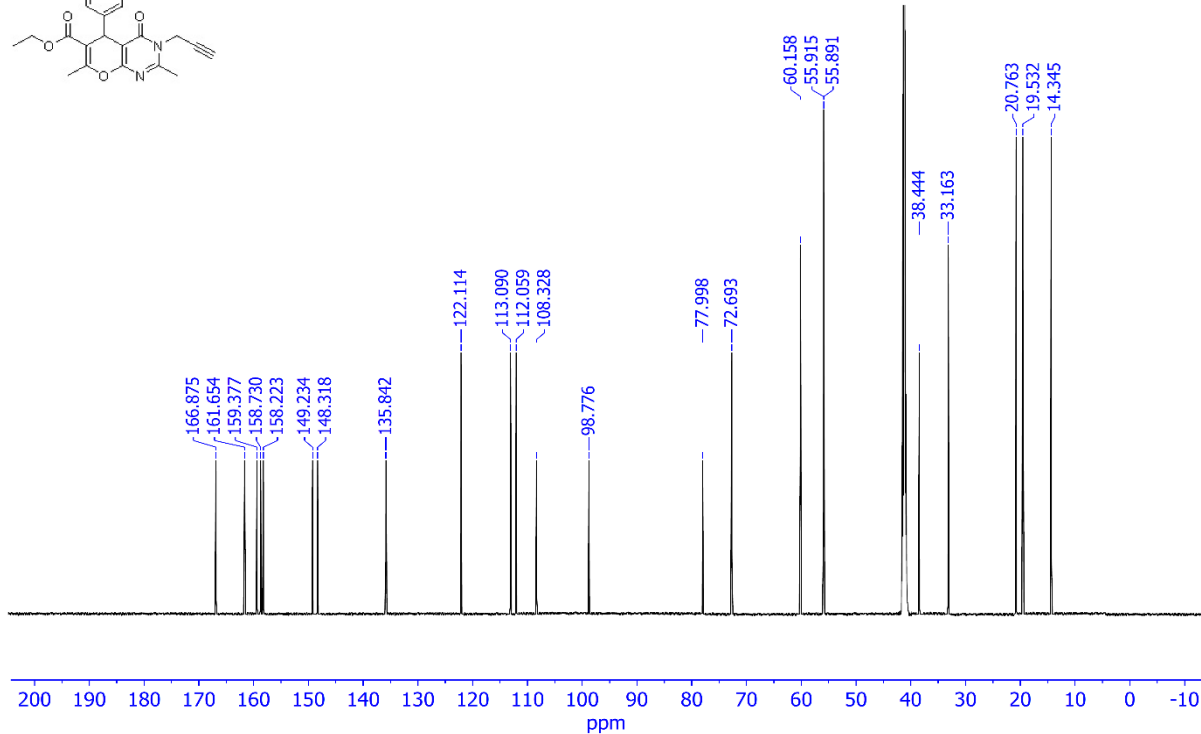
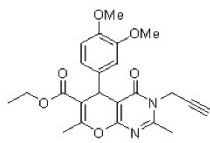
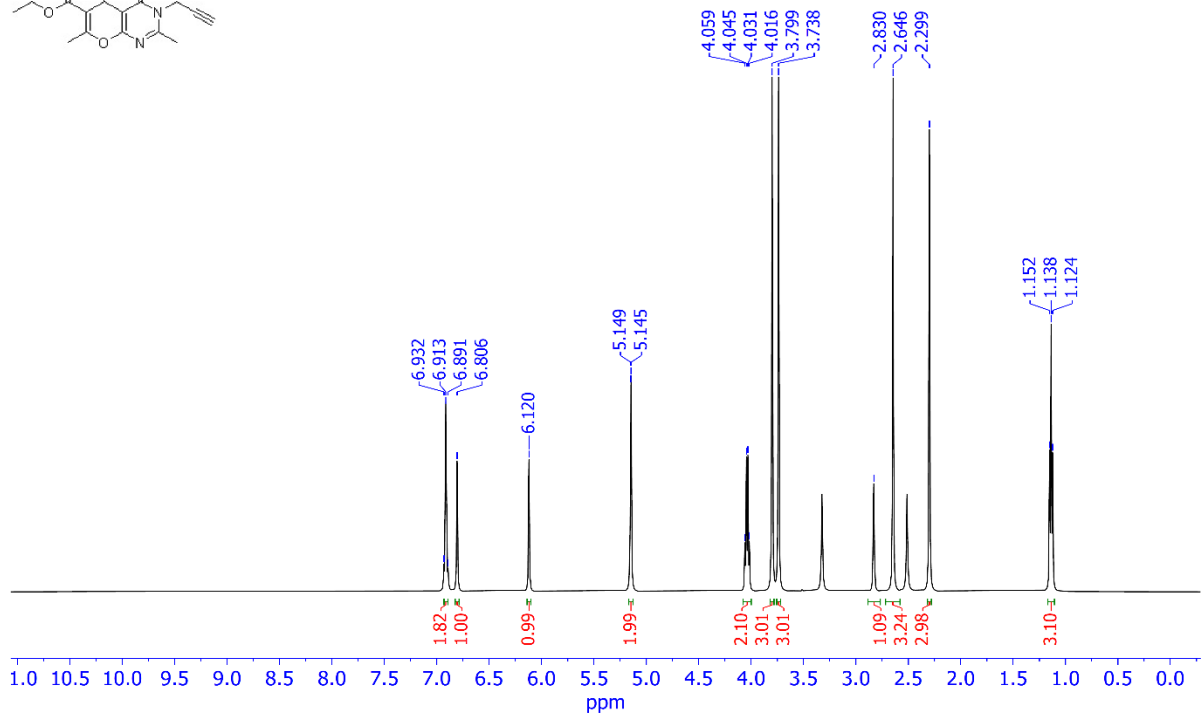
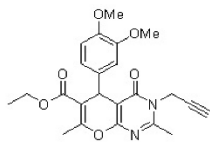


*Ethyl 2,7-dimethyl-5-(4-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6k)*

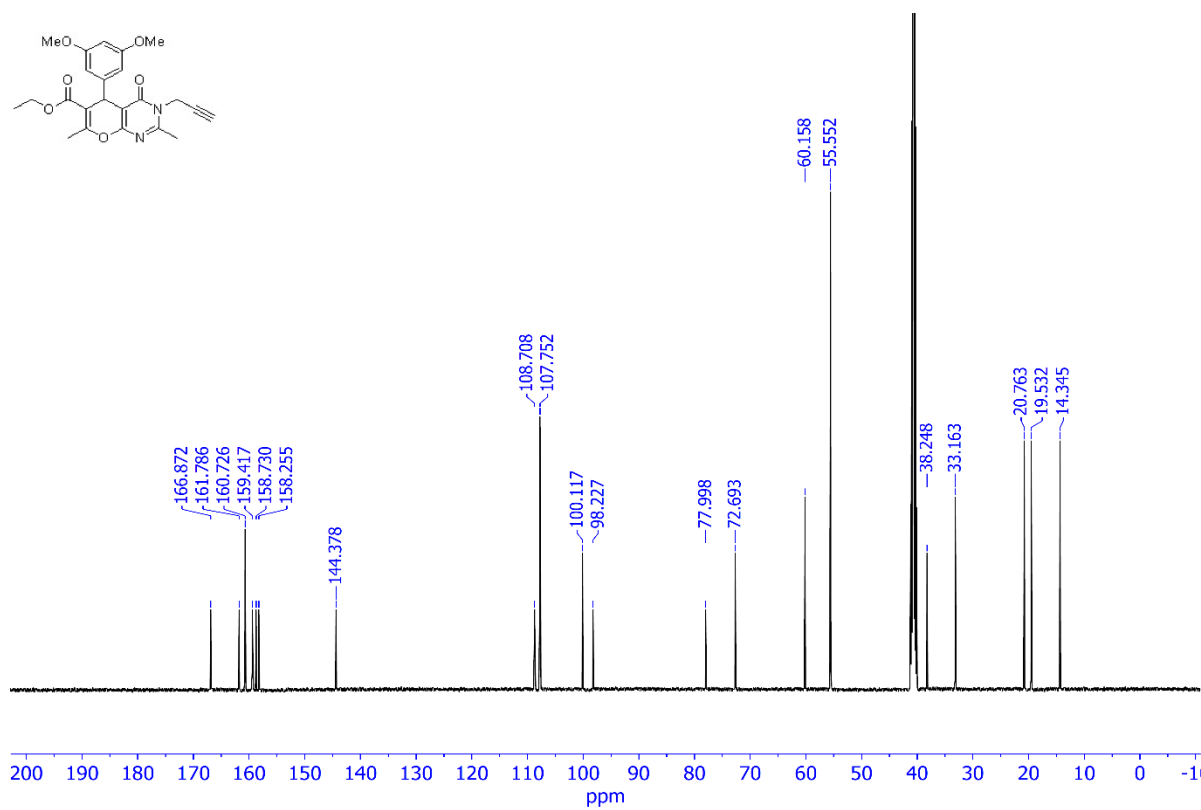
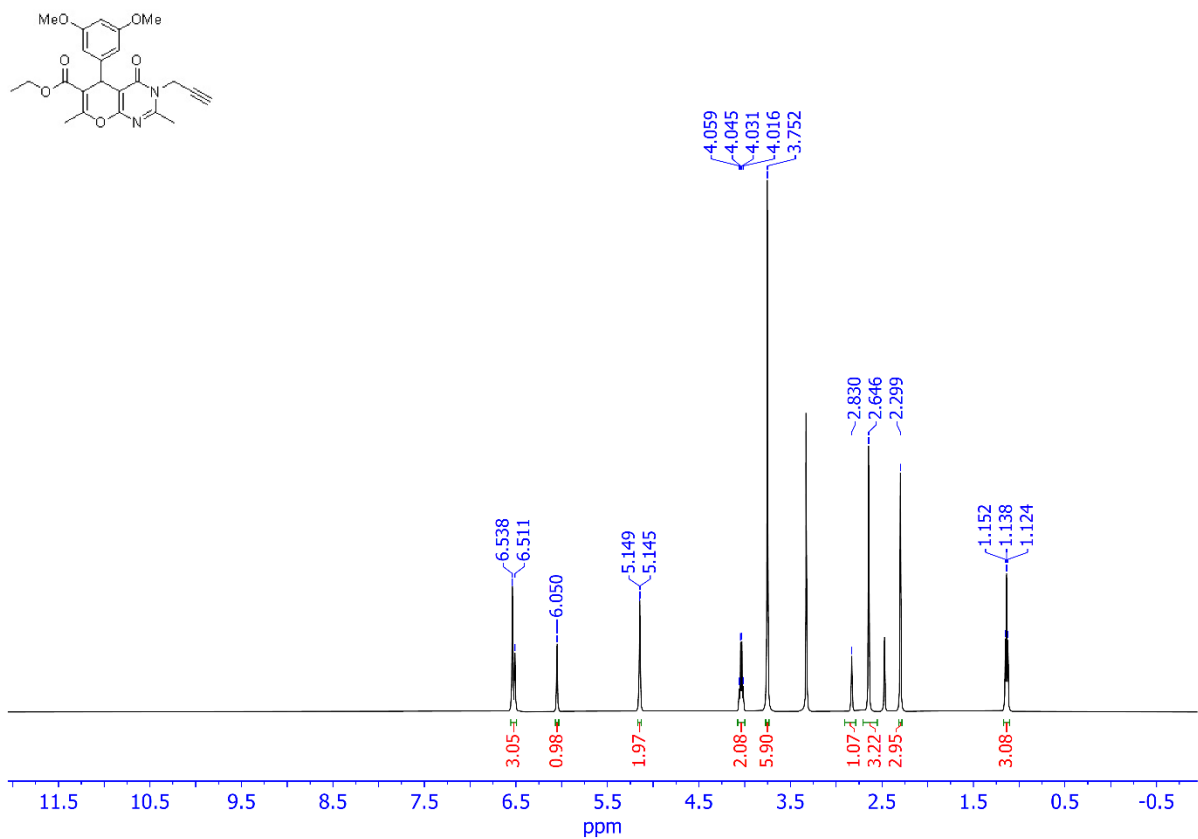




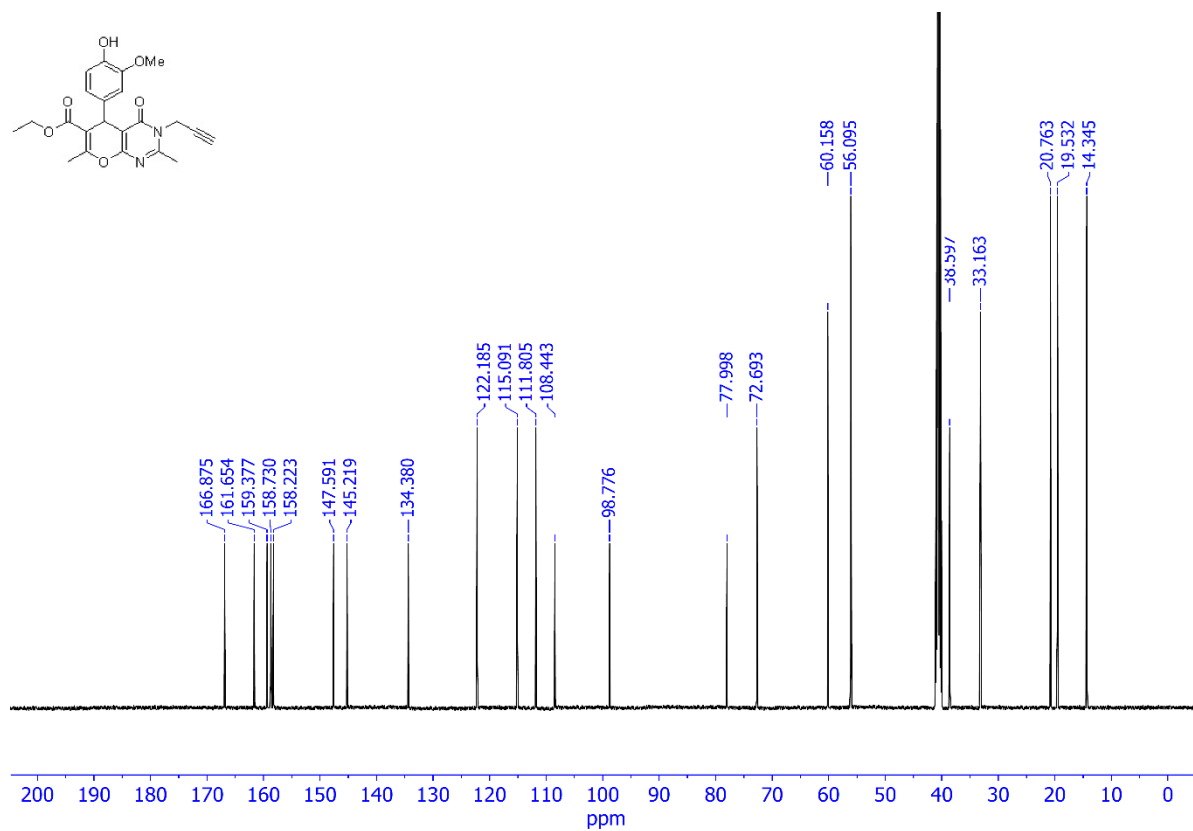
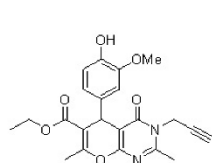
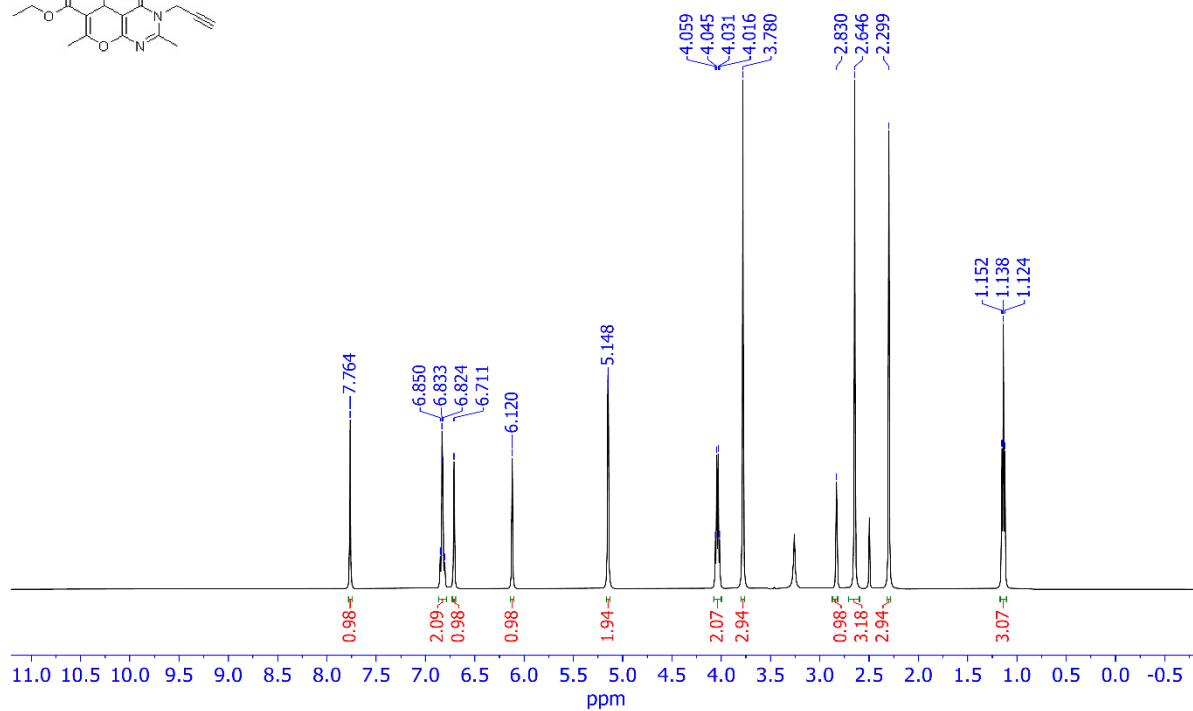
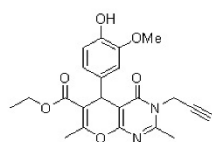
*Ethyl 2,7-dimethyl-5-(3,4-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6m)*



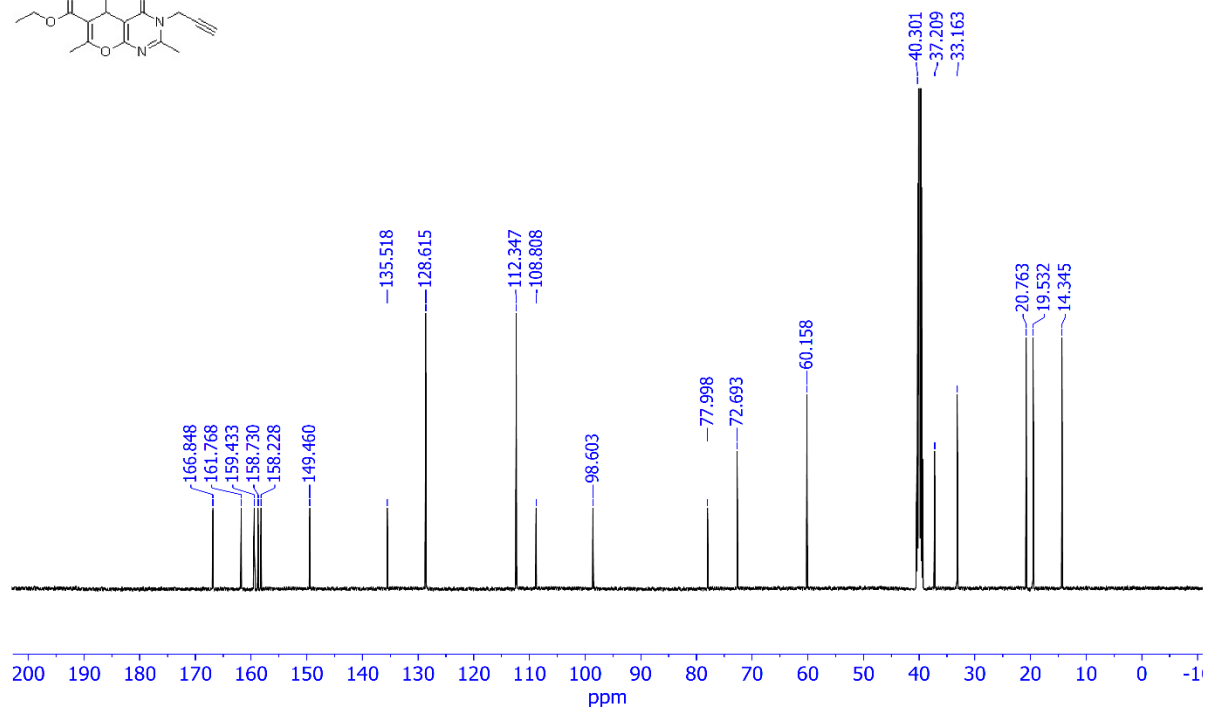
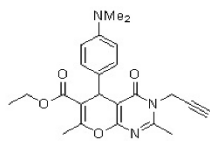
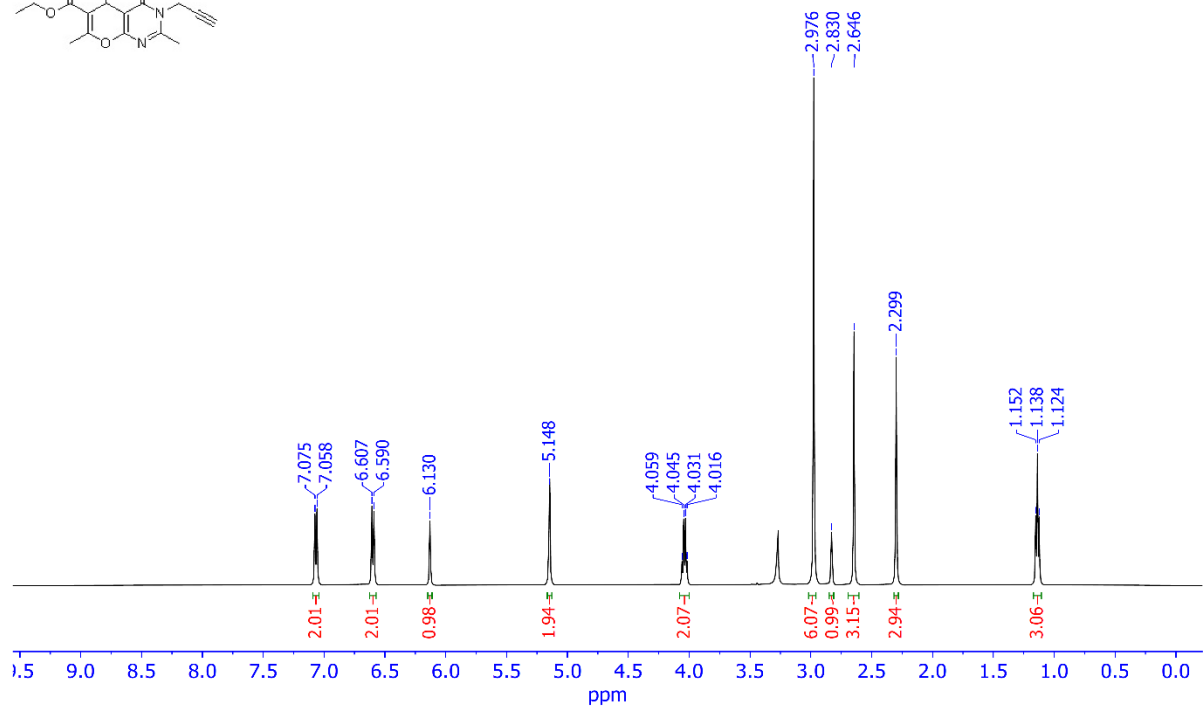
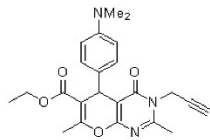
*Ethyl 2,7-dimethyl-5-(3,5-dimethoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylate (6n)*



Ethyl 2,7-dimethyl-5-(4-hydroxy-3-methoxyphenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (**60**)



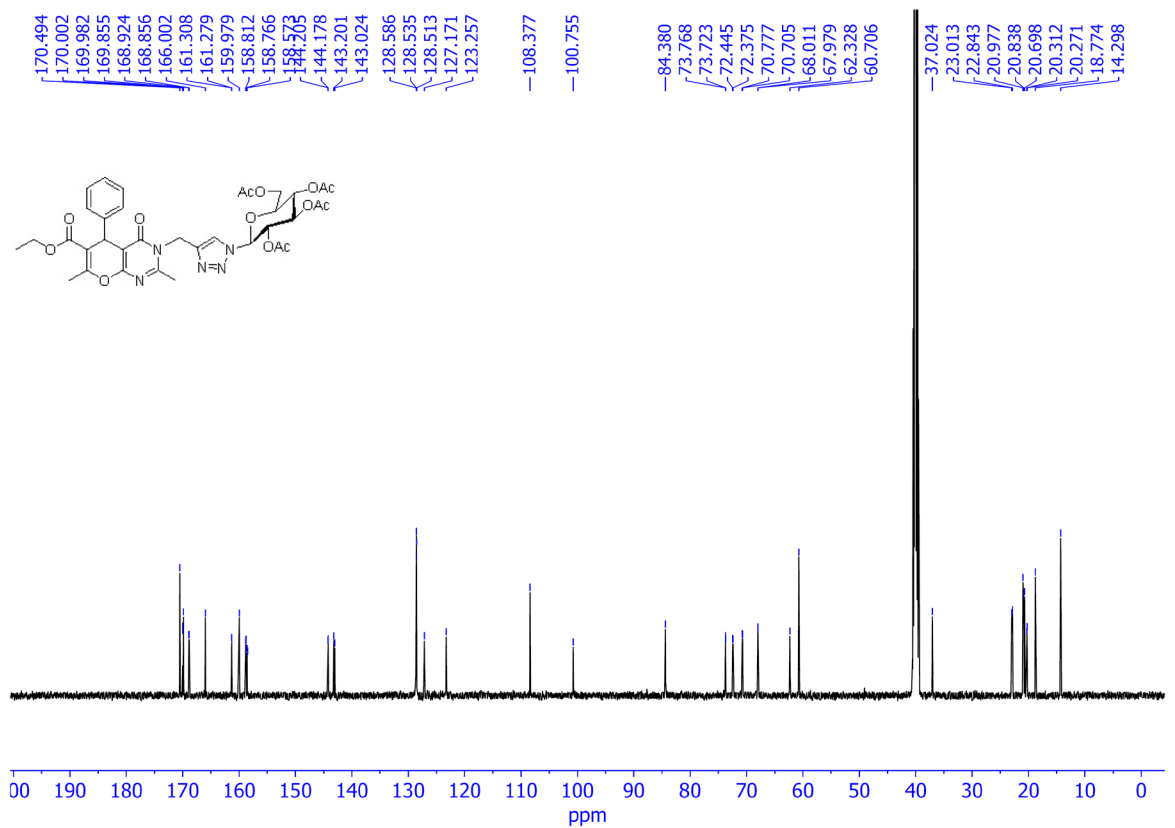
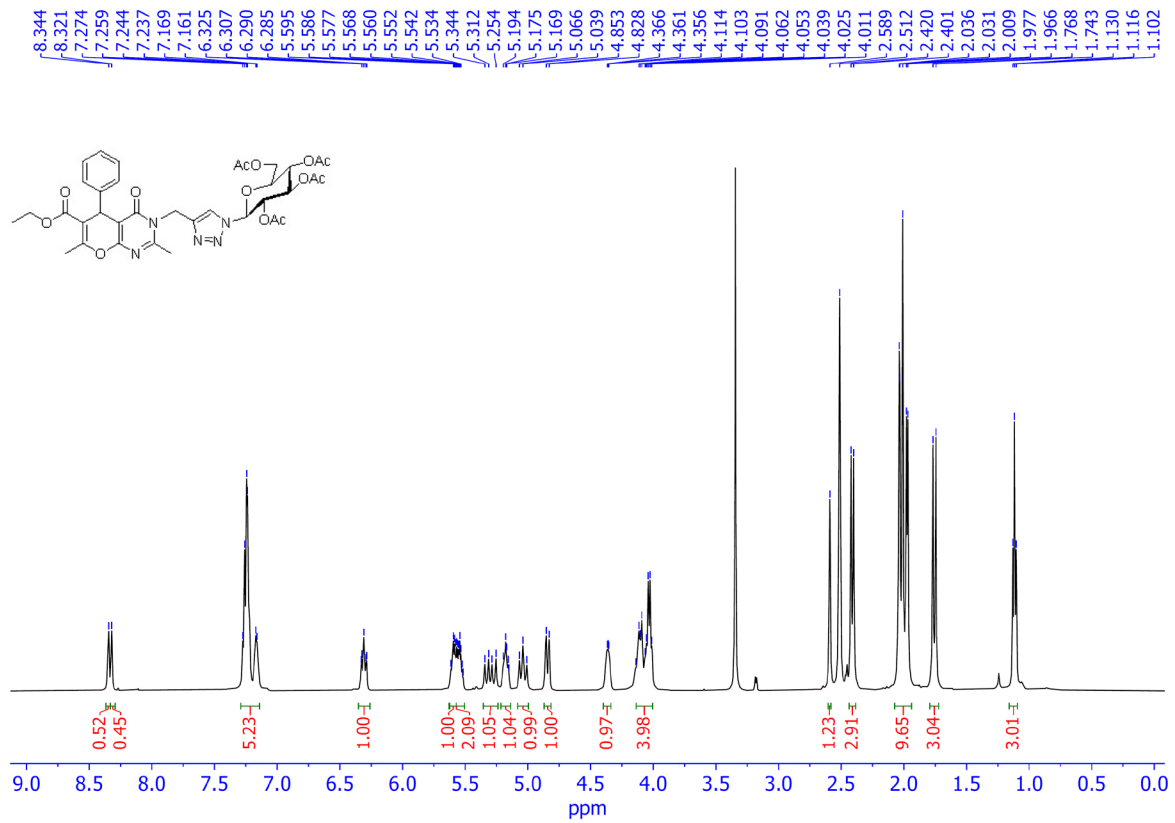
*Ethyl 2,7-dimethyl-5-(4-dimethylaminophenyl)-4-oxo-3-propargyl-3,5-dihydro-4H-pyrano[2,3-d]pyrimidine-6-carboxylates (6p)*

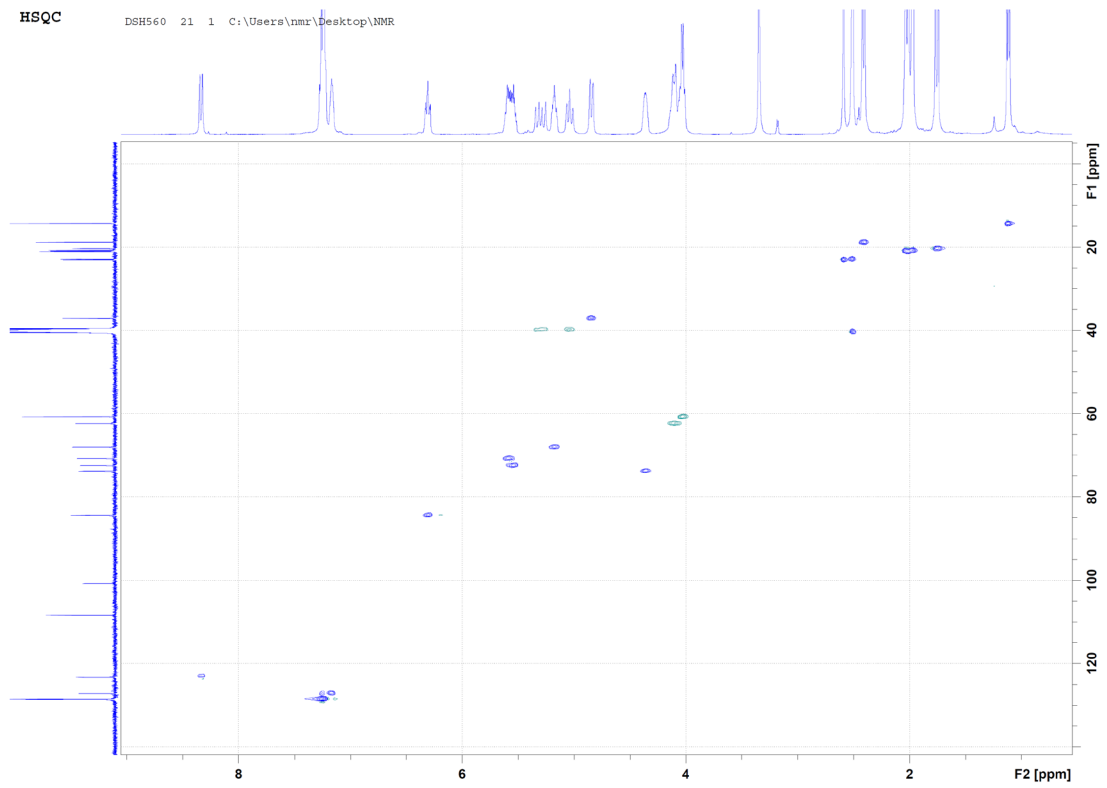
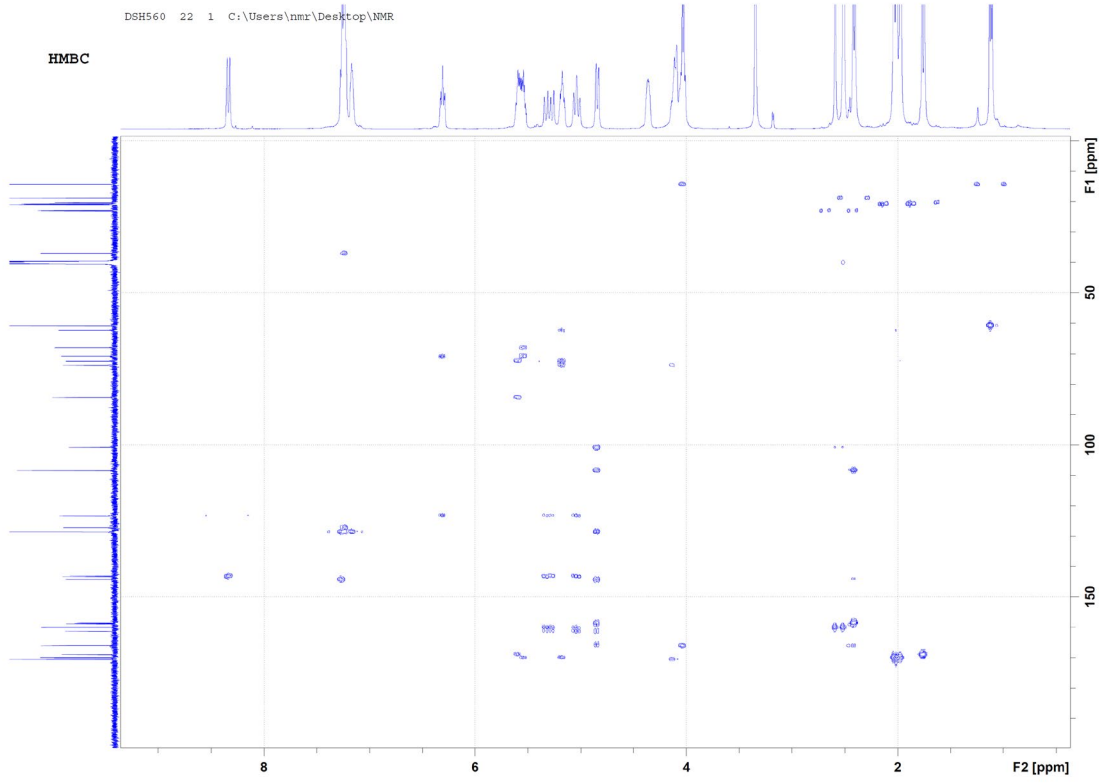


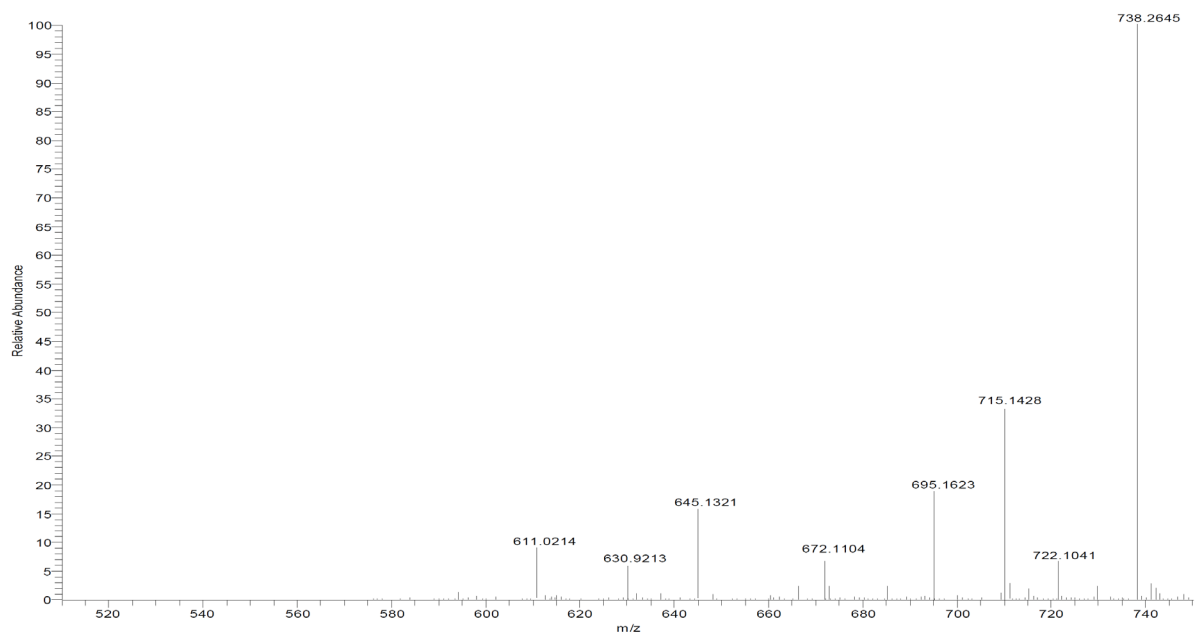
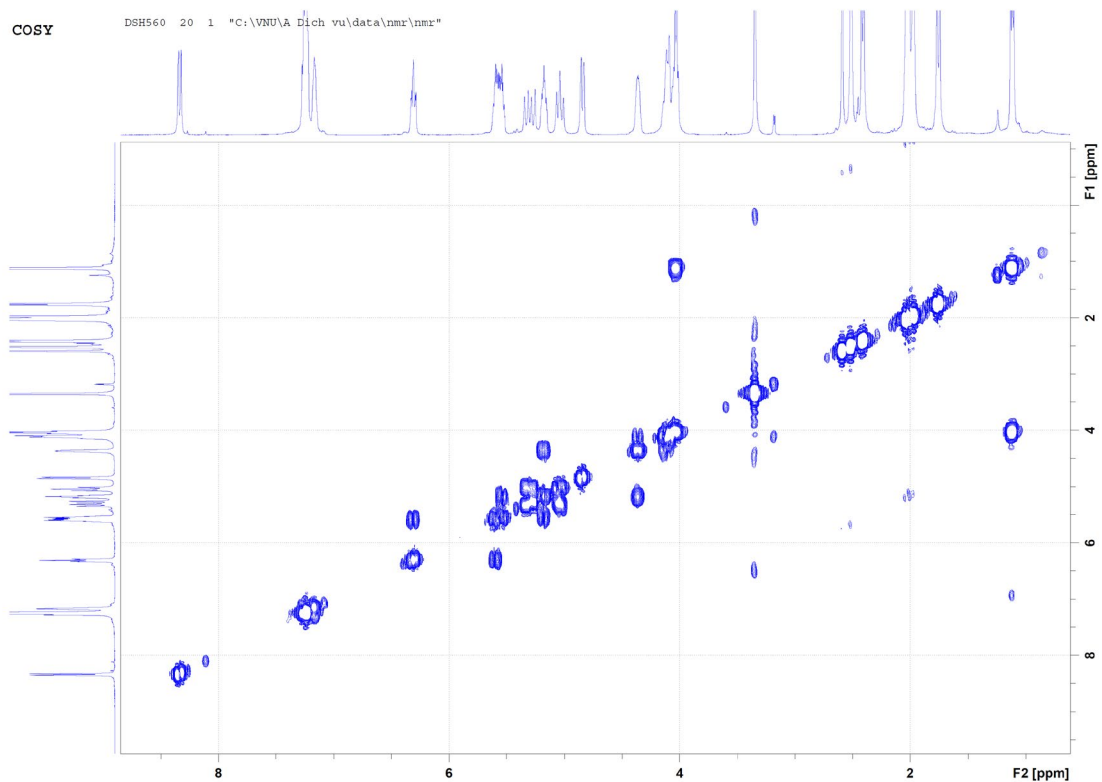
## 6. NMR and selected mass spectra of compounds 8a-8s

*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-phenyl-4-oxo-3,5-dihydro-4H-pyran[2,3-d]pyrimidin-6-carboxylate (8a)*

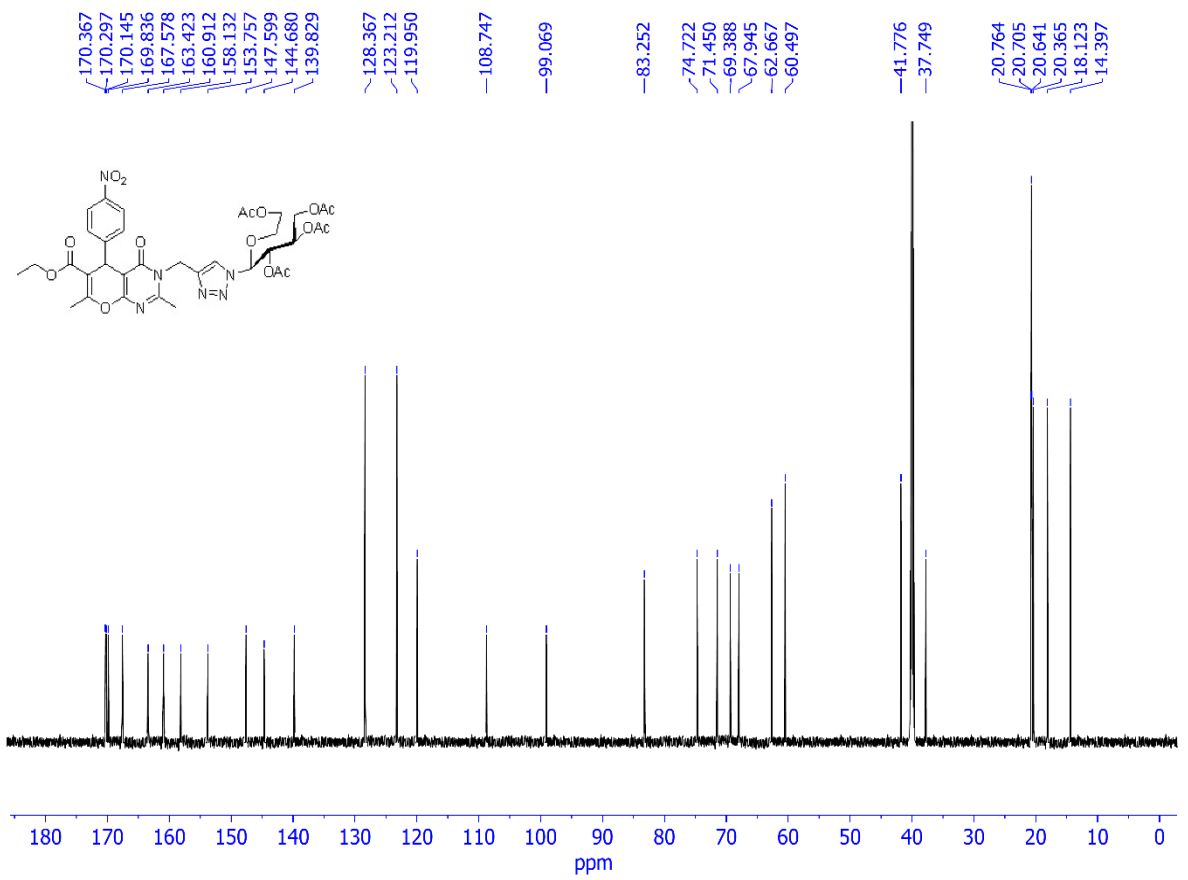
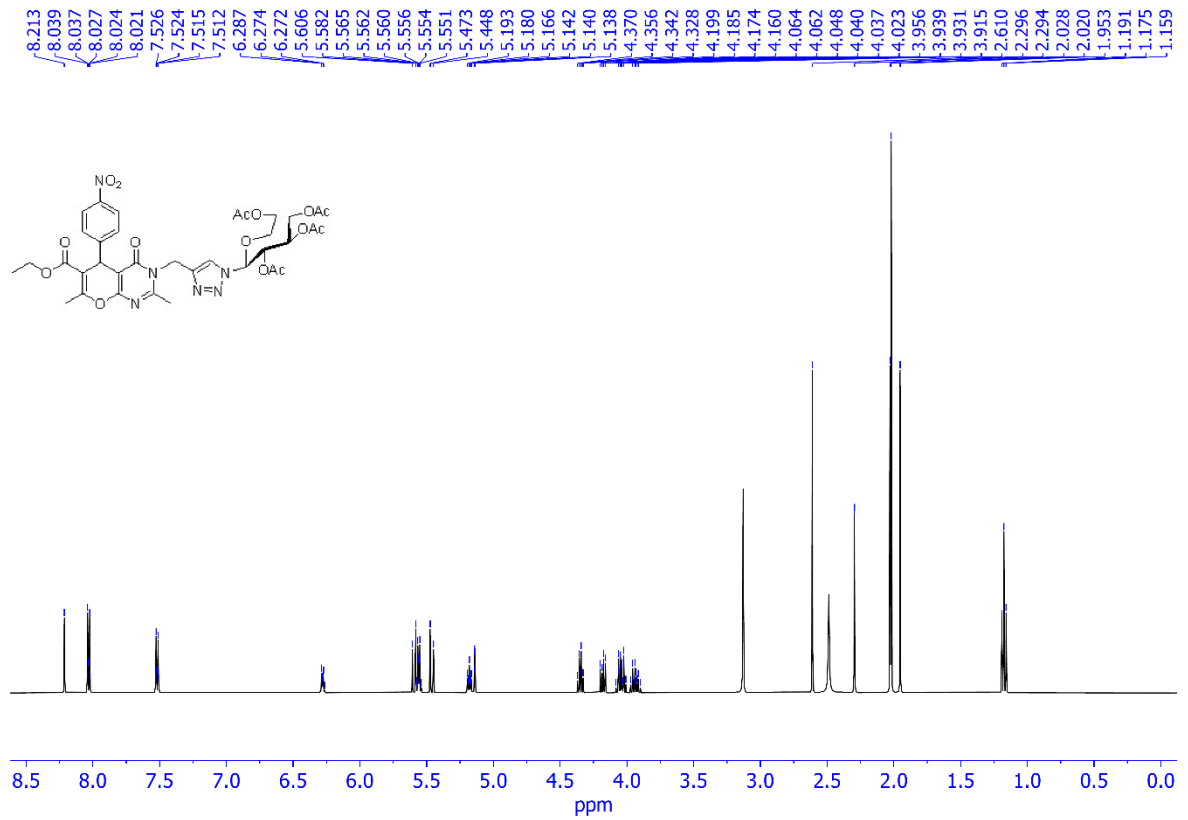


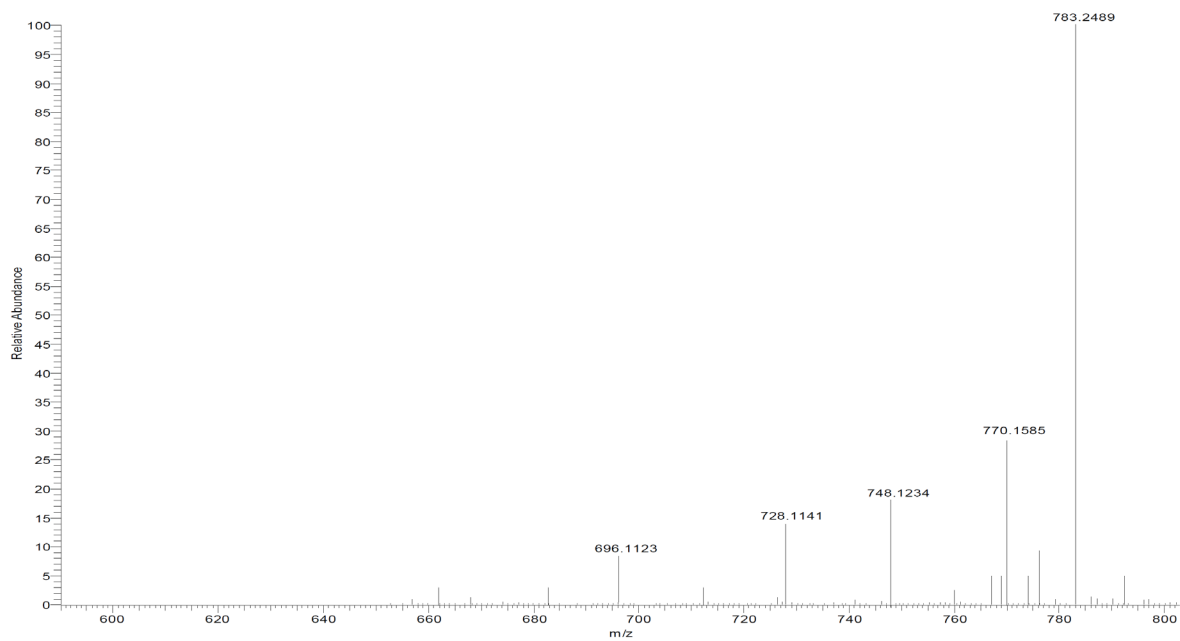




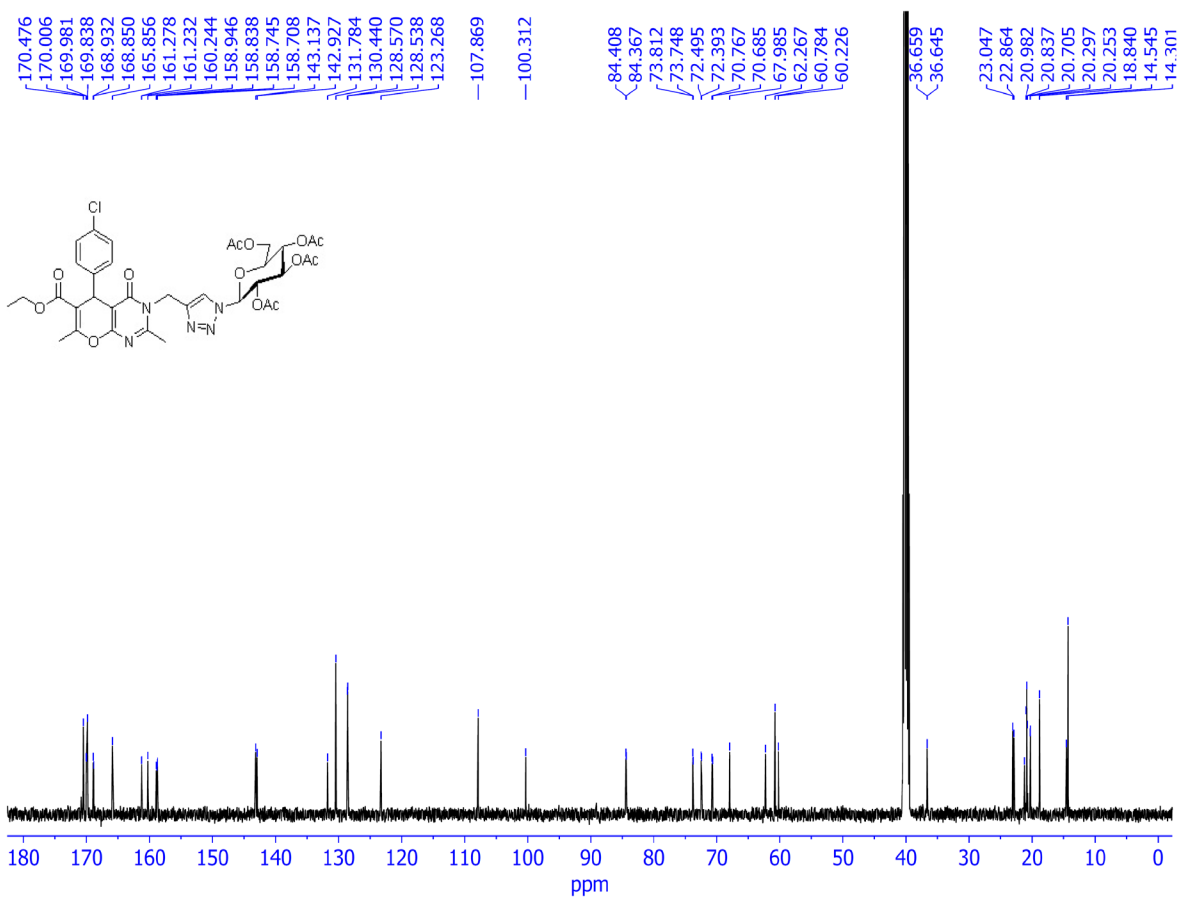
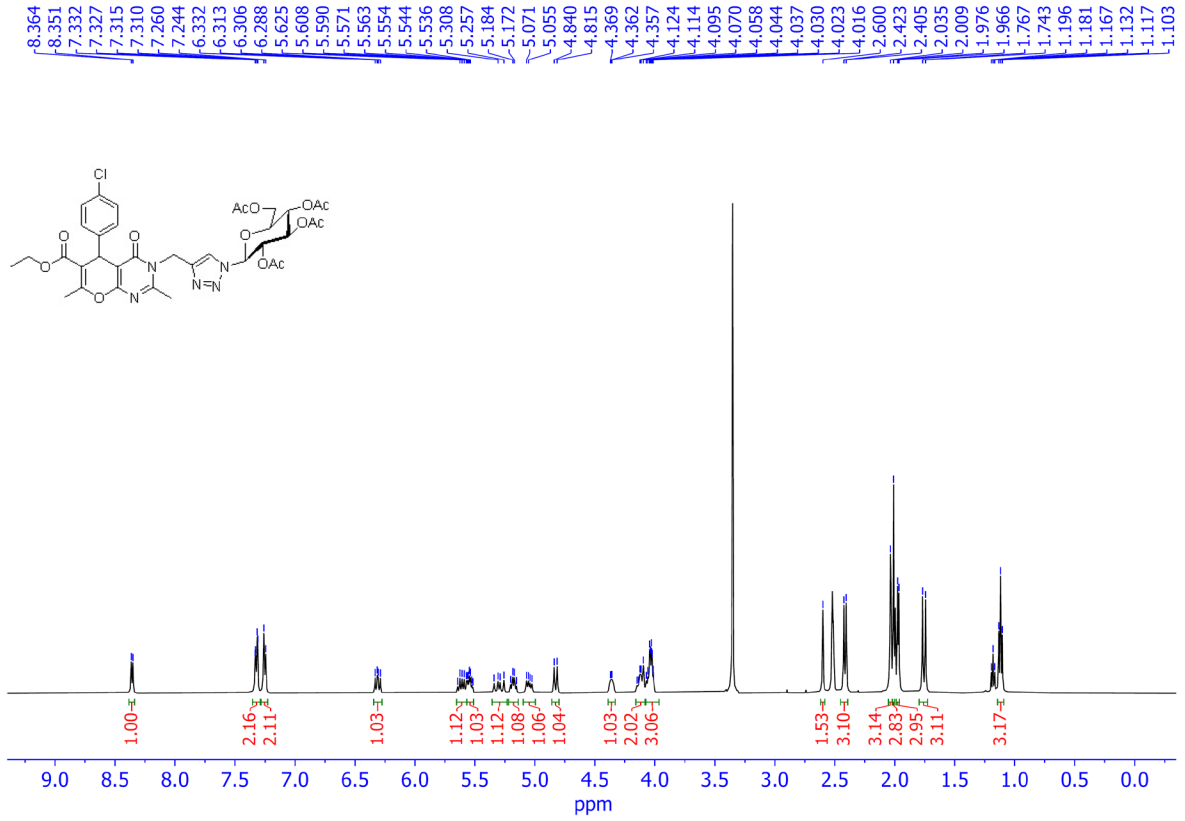


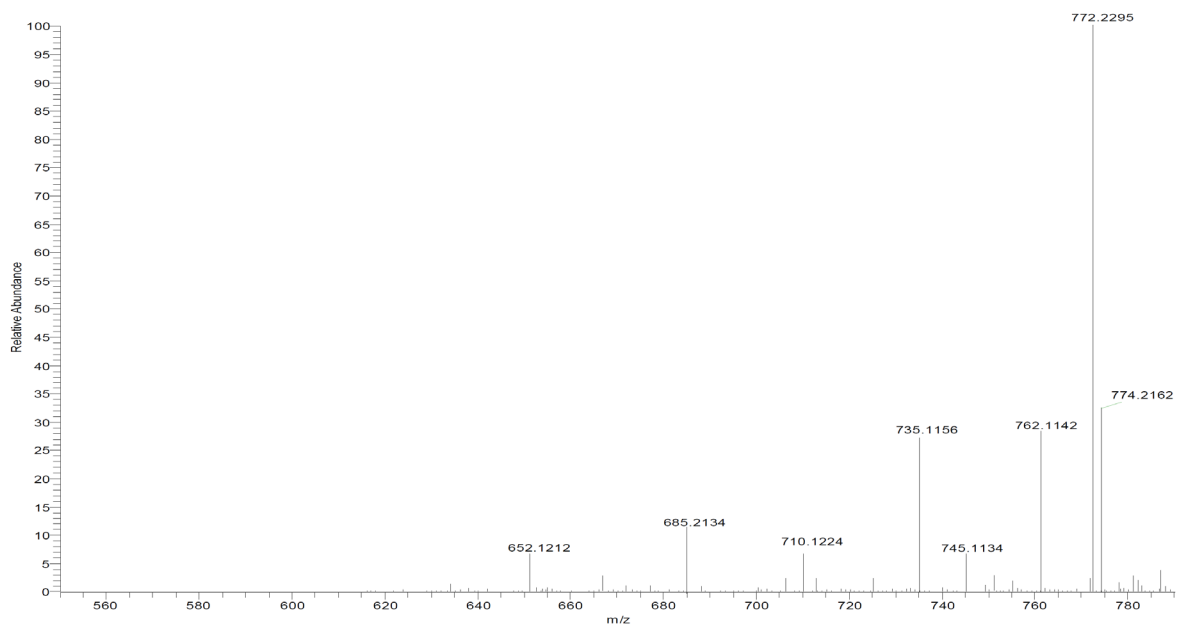
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8b)*



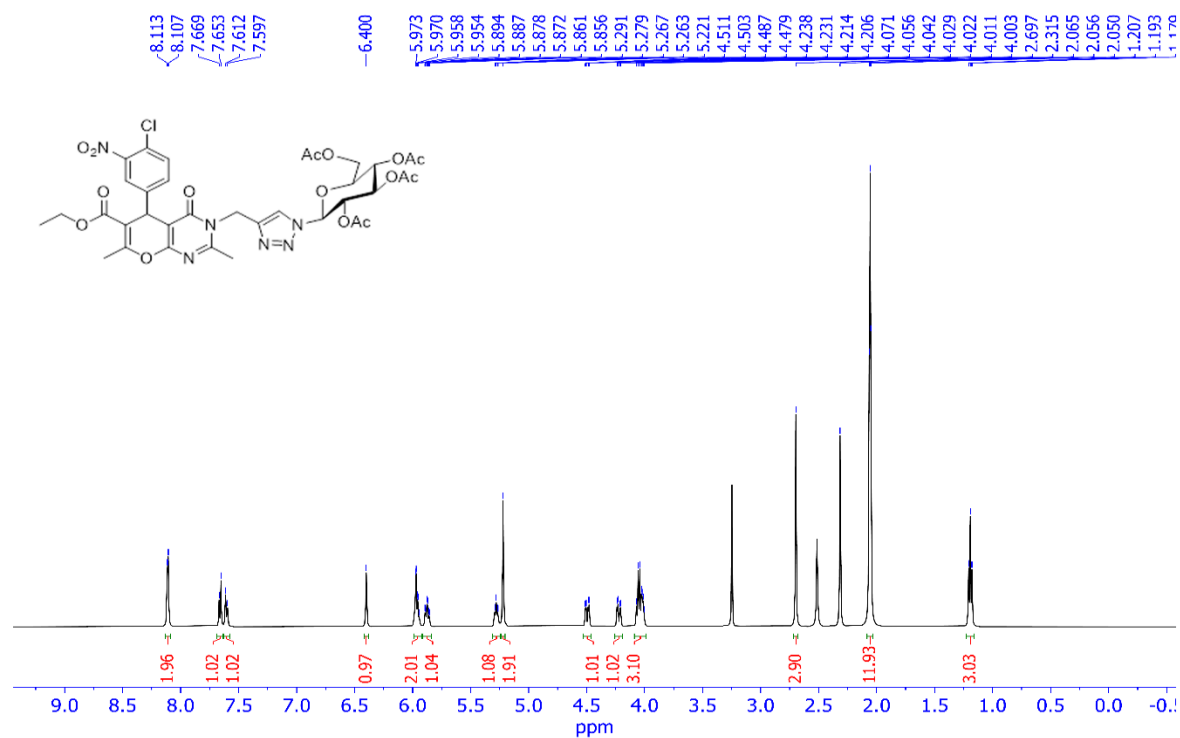


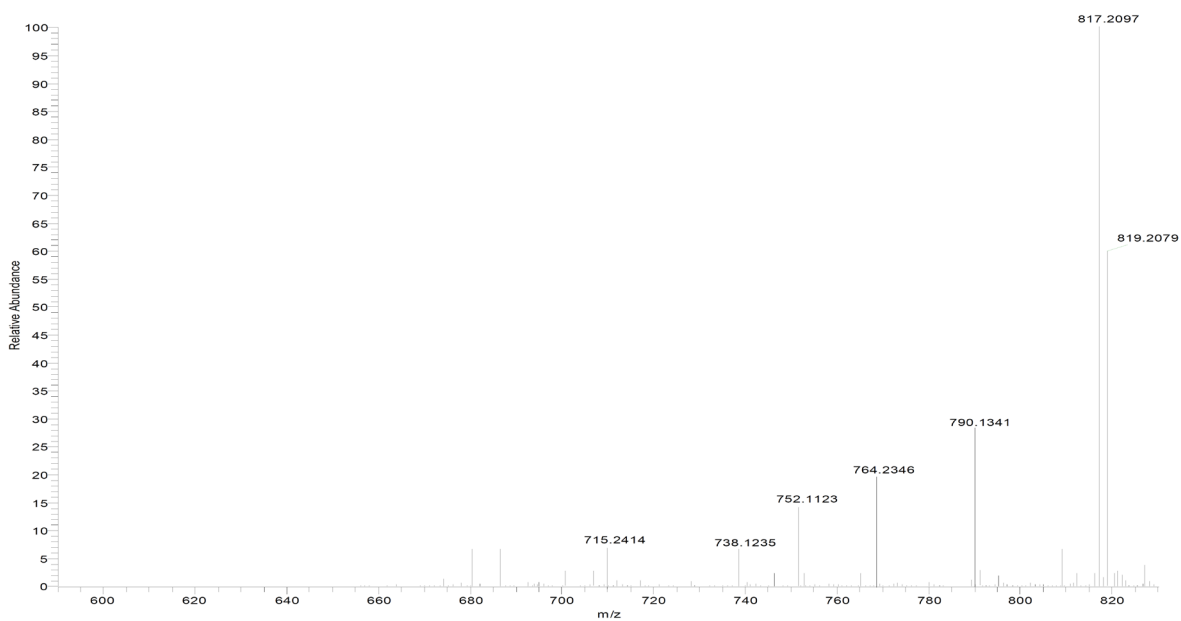
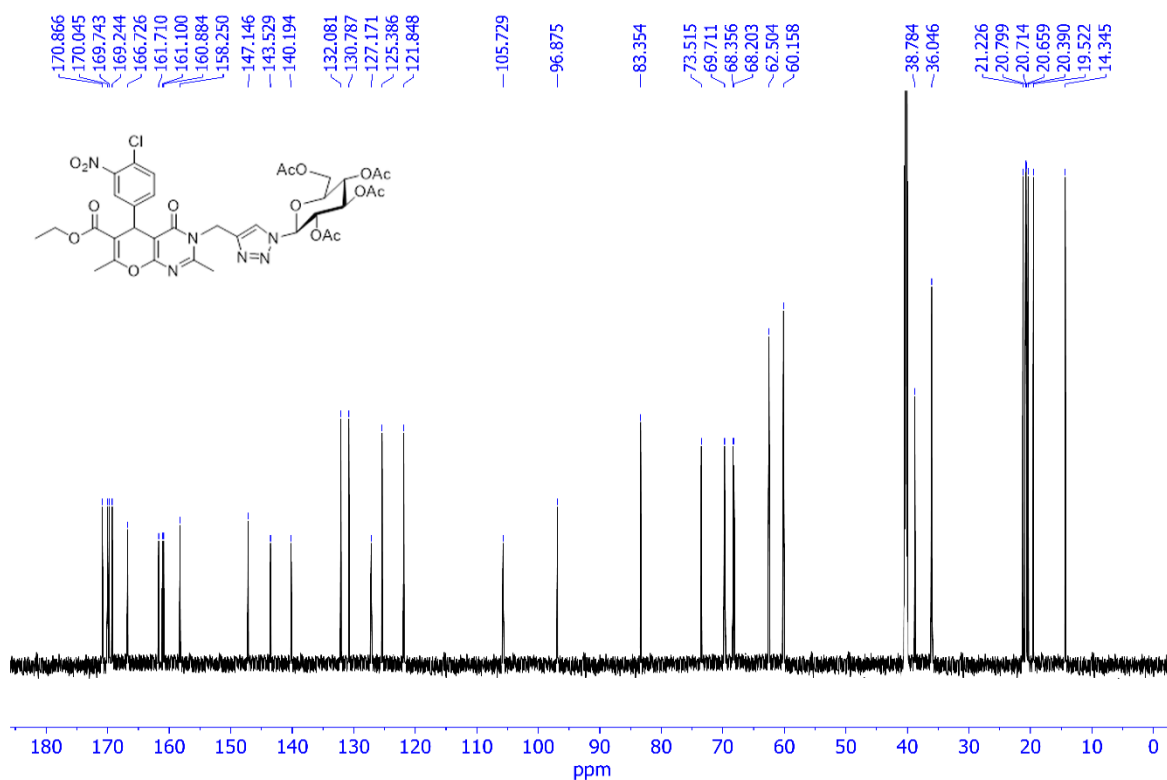
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-chlorophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8c)*





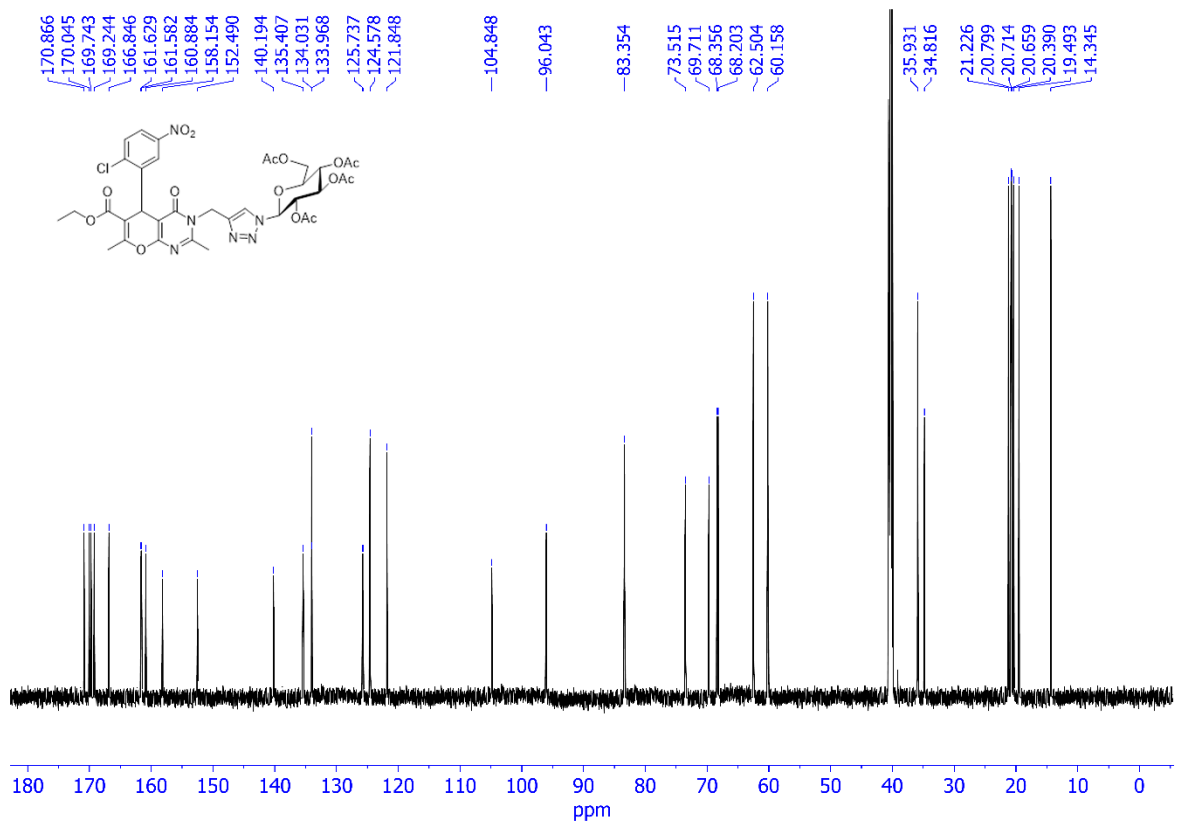
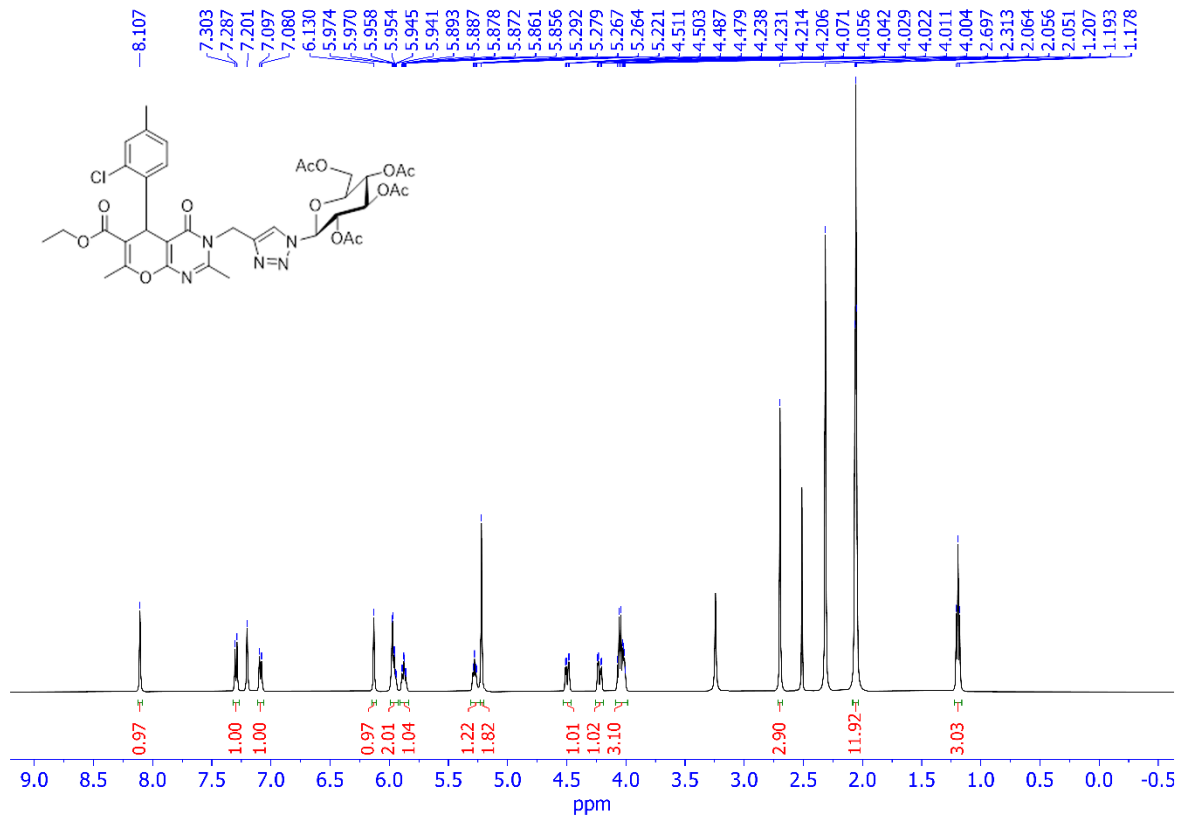
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-chloro-3-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8d)*

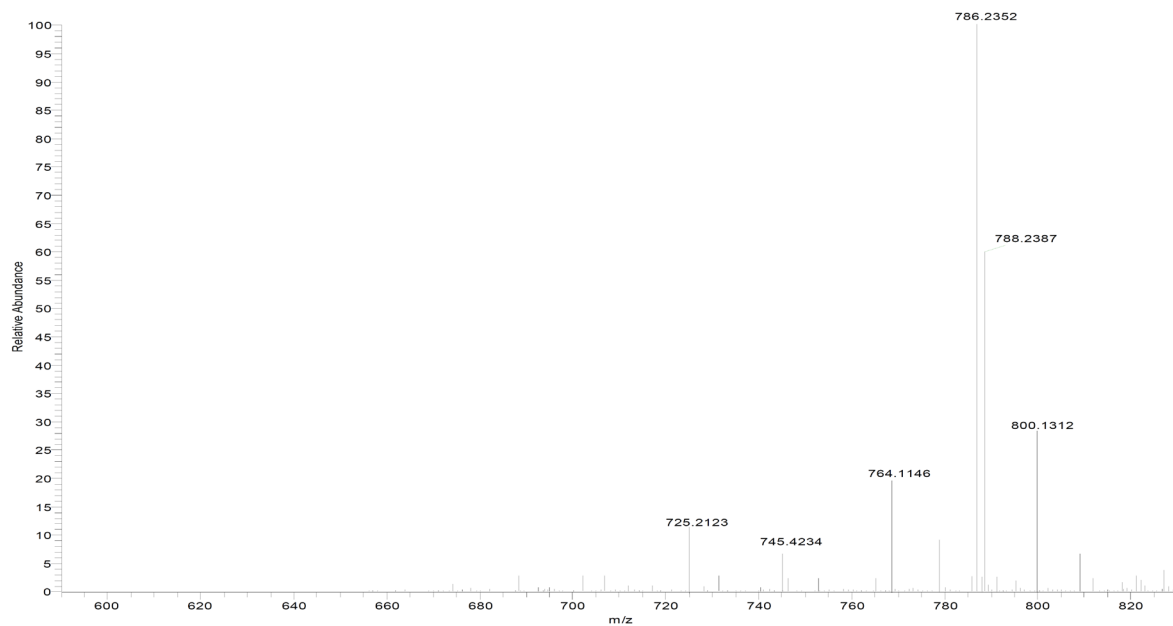




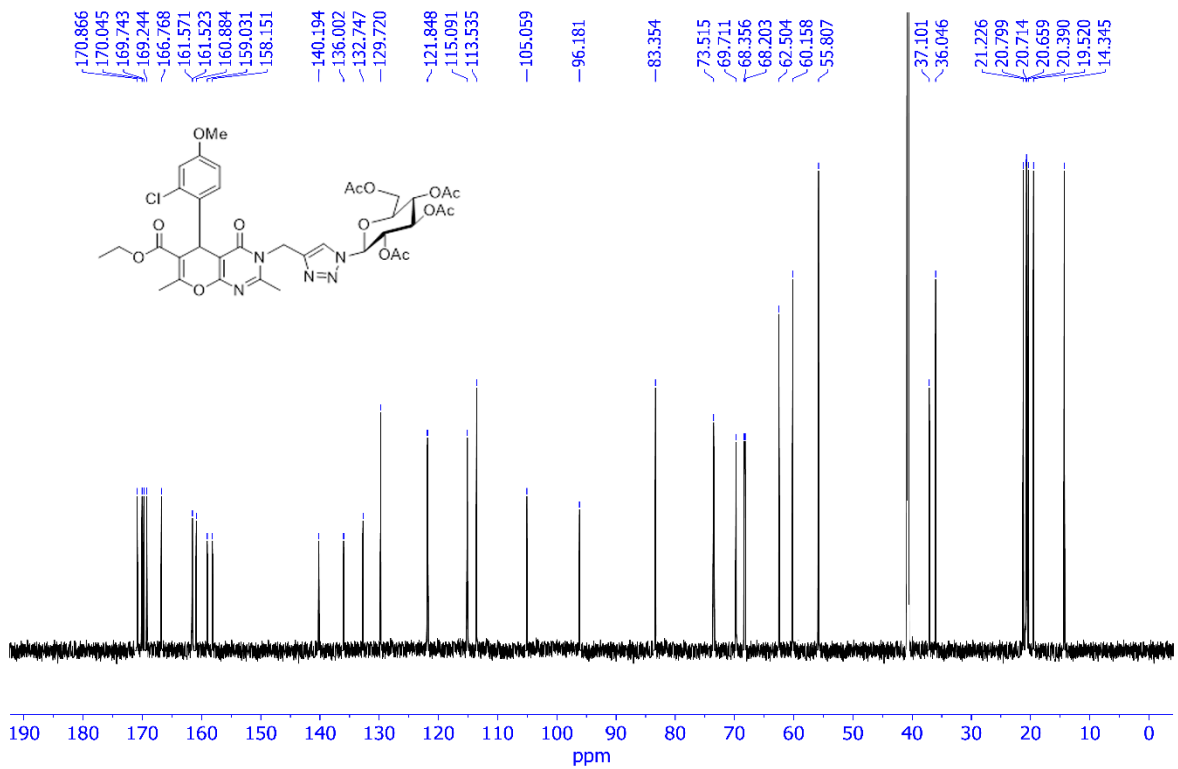
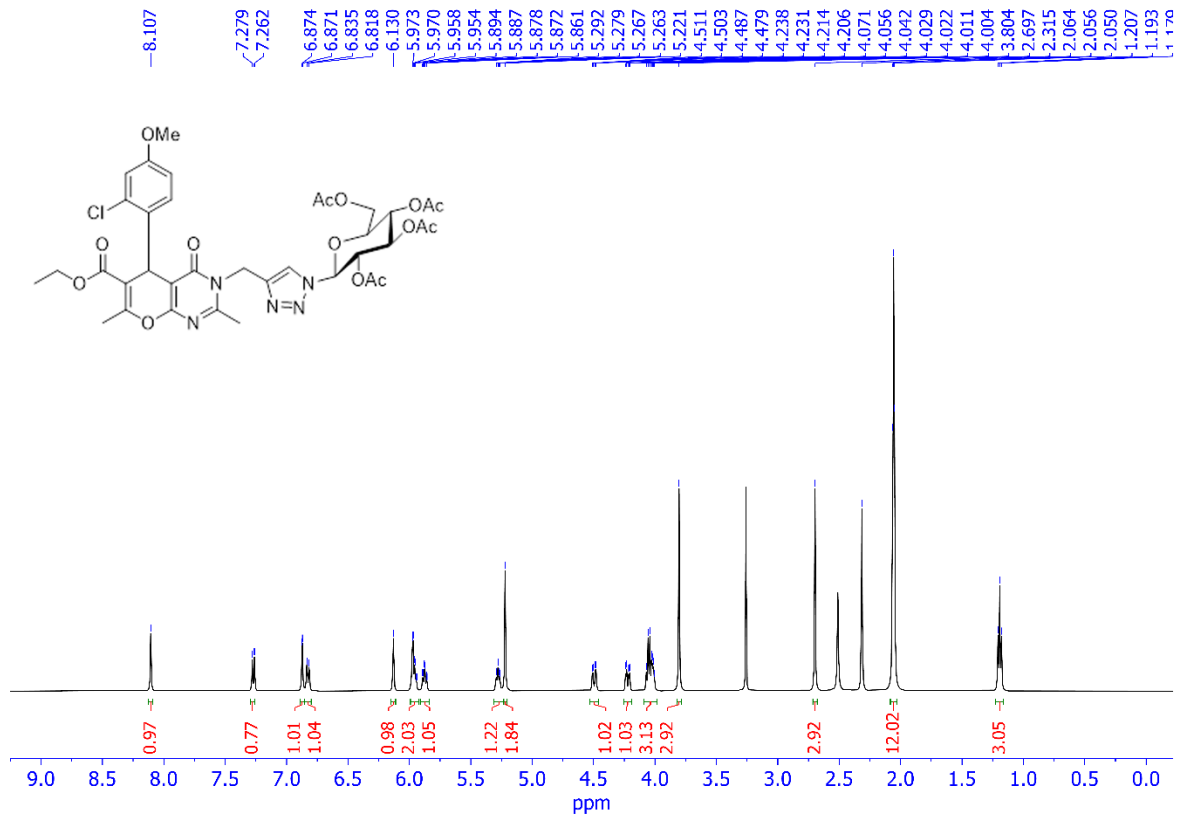
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2-chloro-4-methylphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (**8e**)*

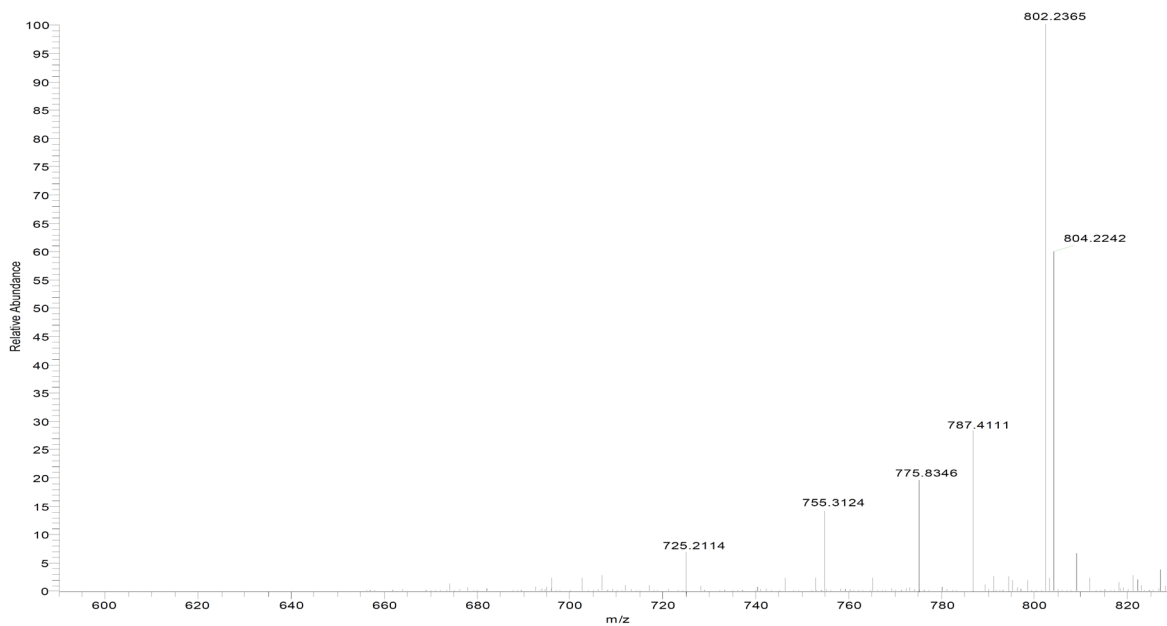




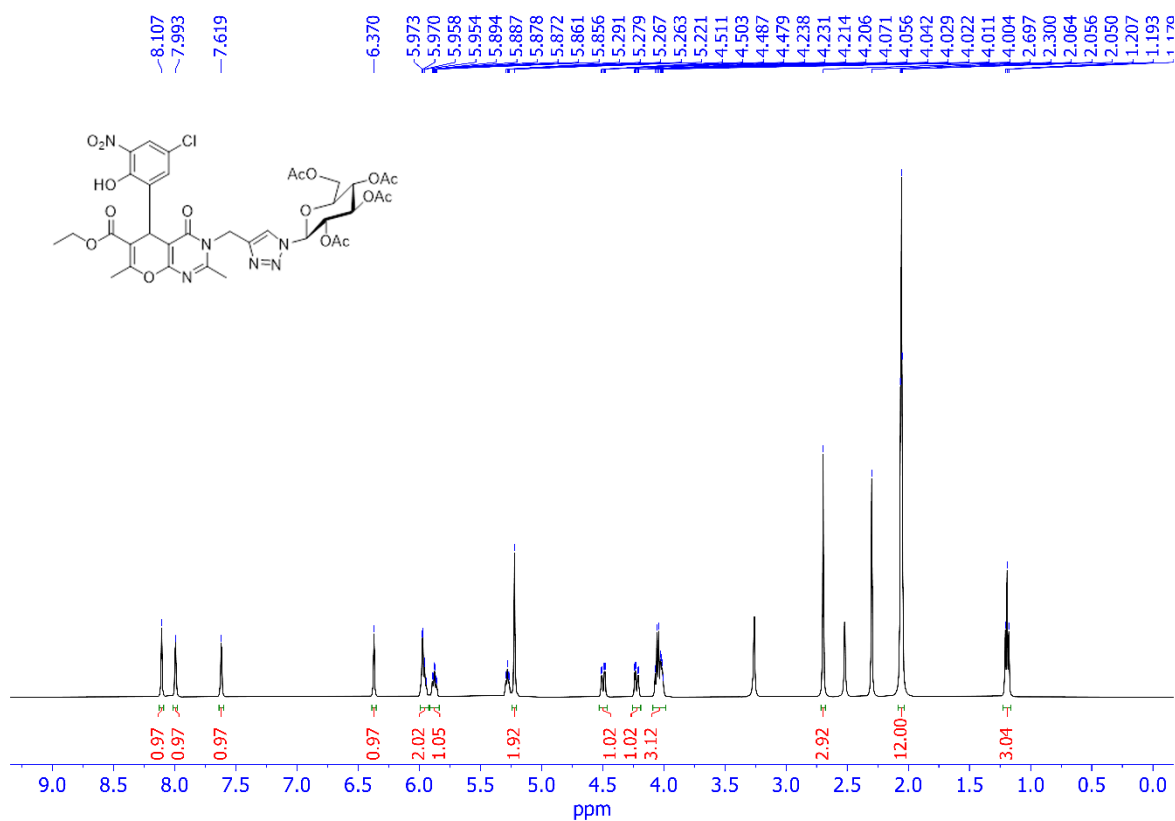


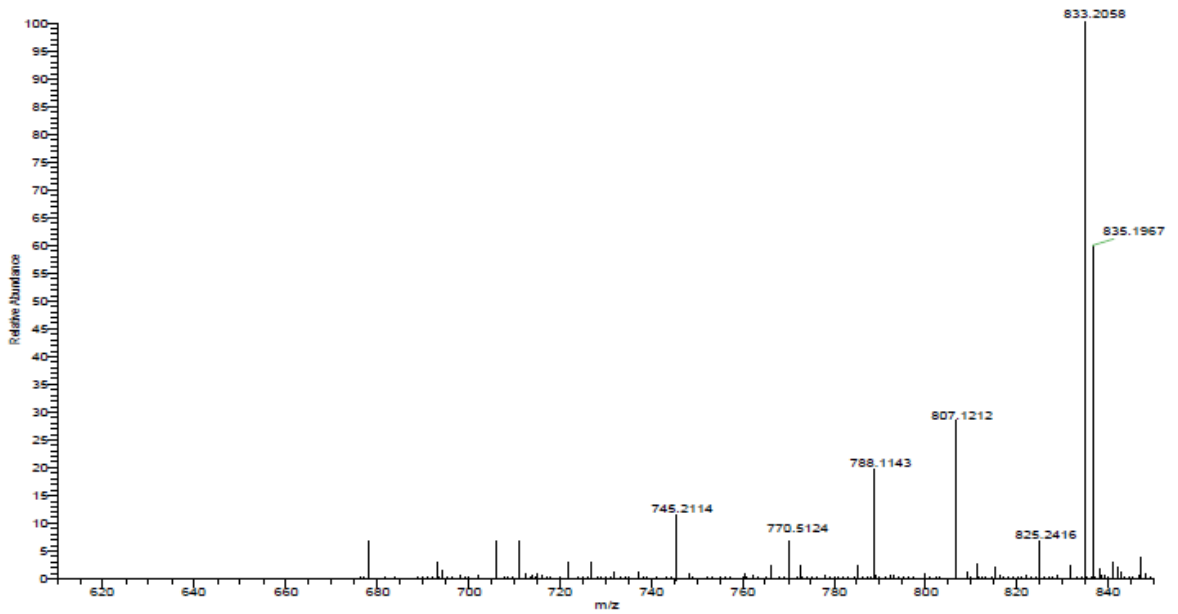
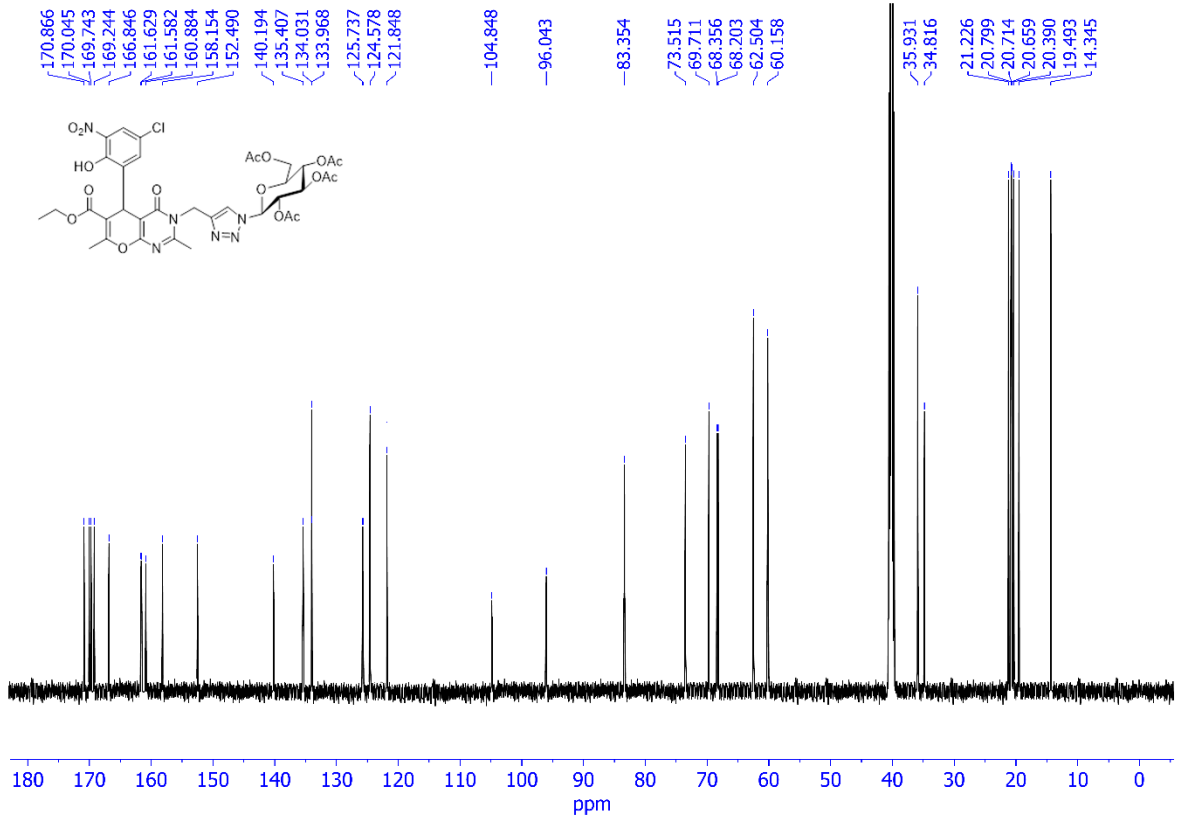
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2-chloro-4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8f)*



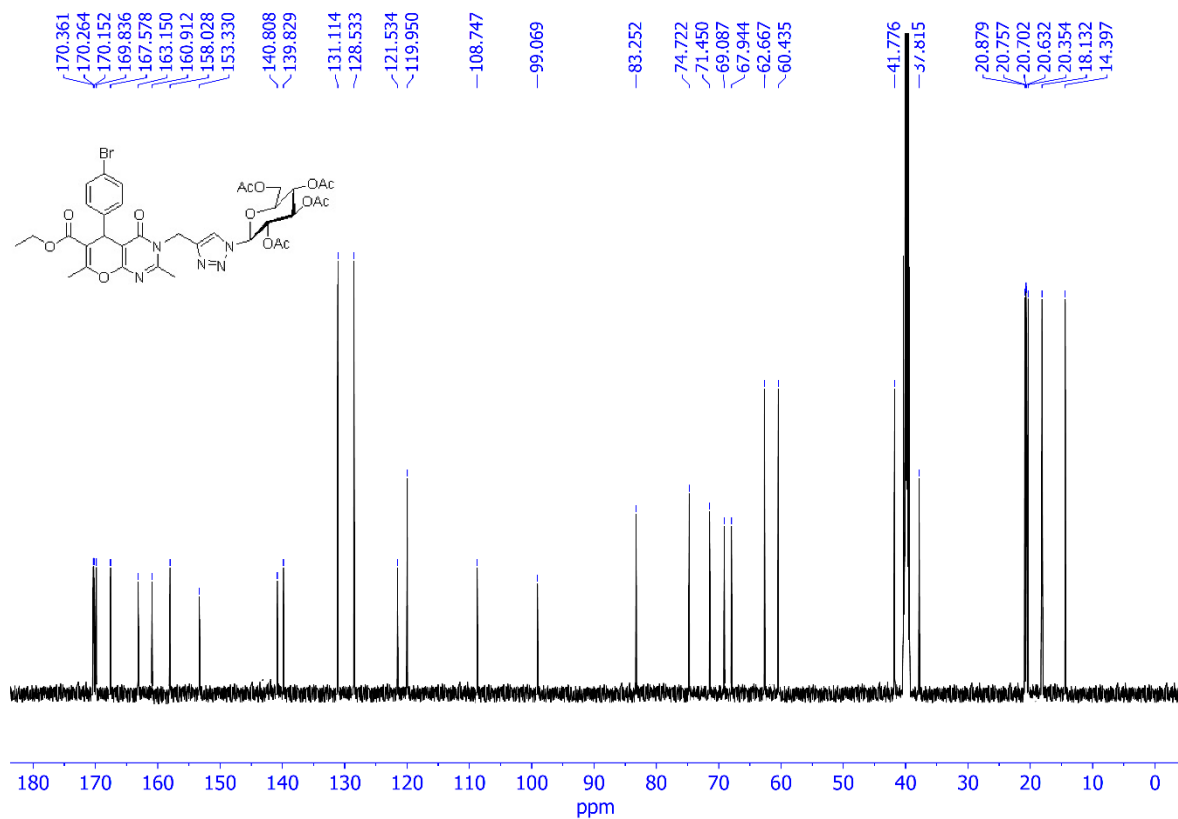
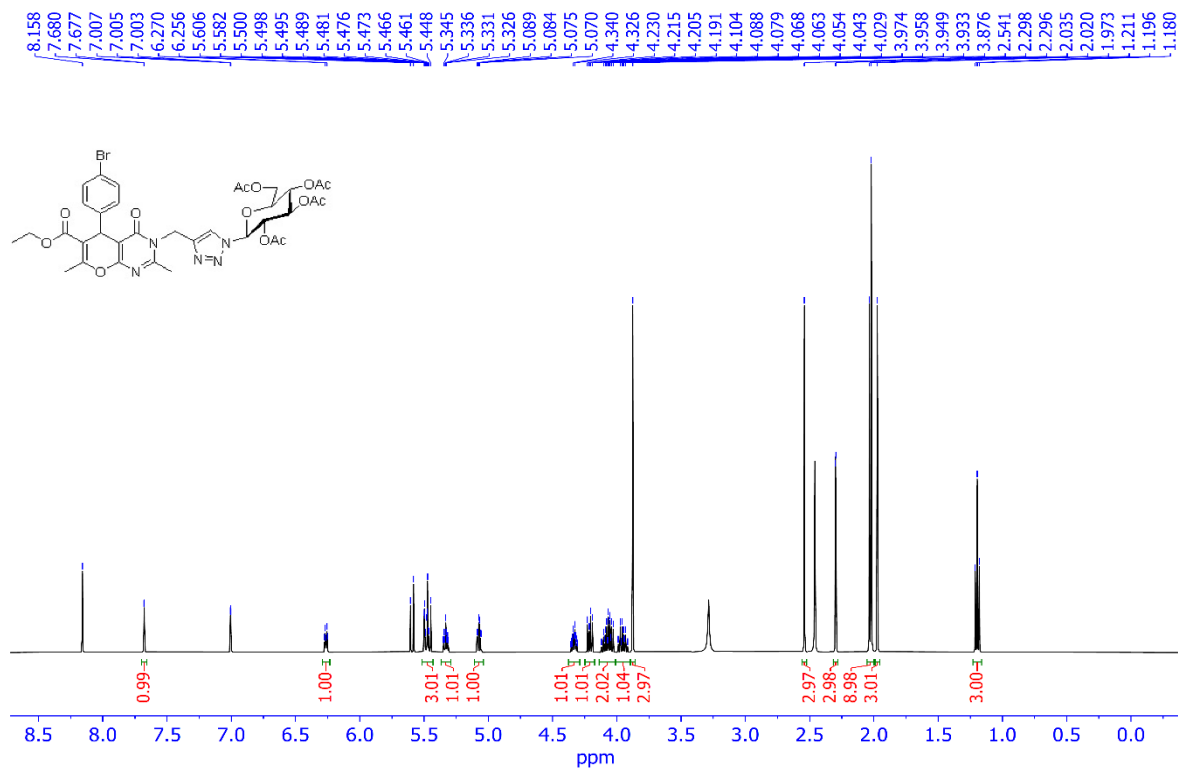


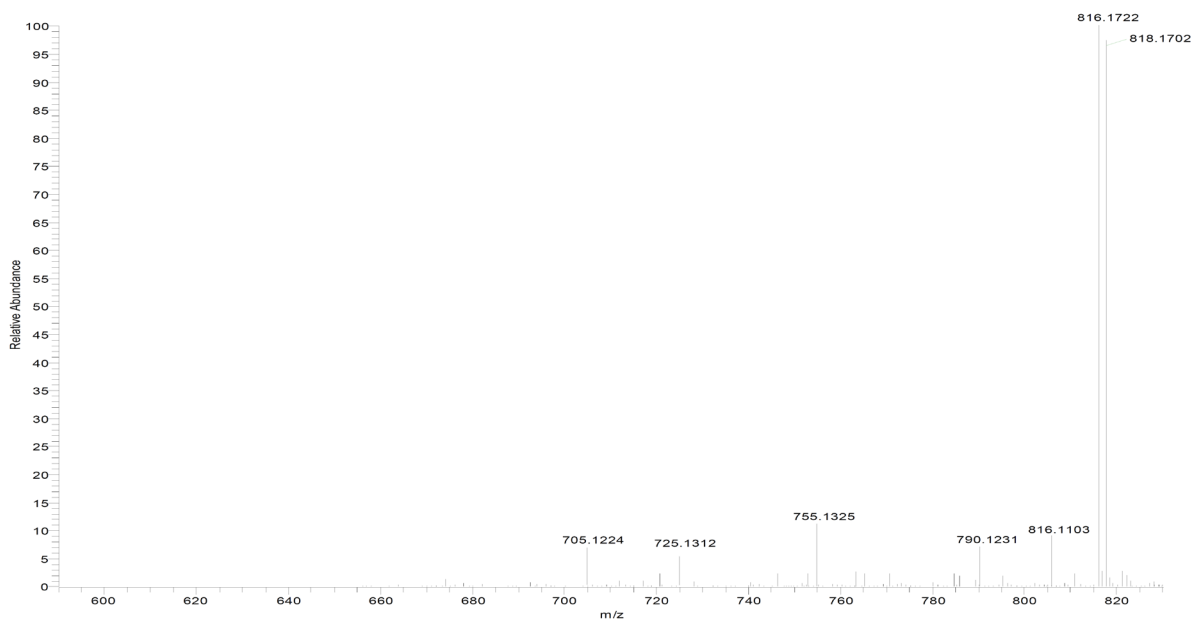
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(5-chloro-2-hydroxy-3-nitrophenyl)-4-oxo-3,5-dihydro-4H-pyran[2,3-d]pyrimidin-6-carboxylate (**8g**)*



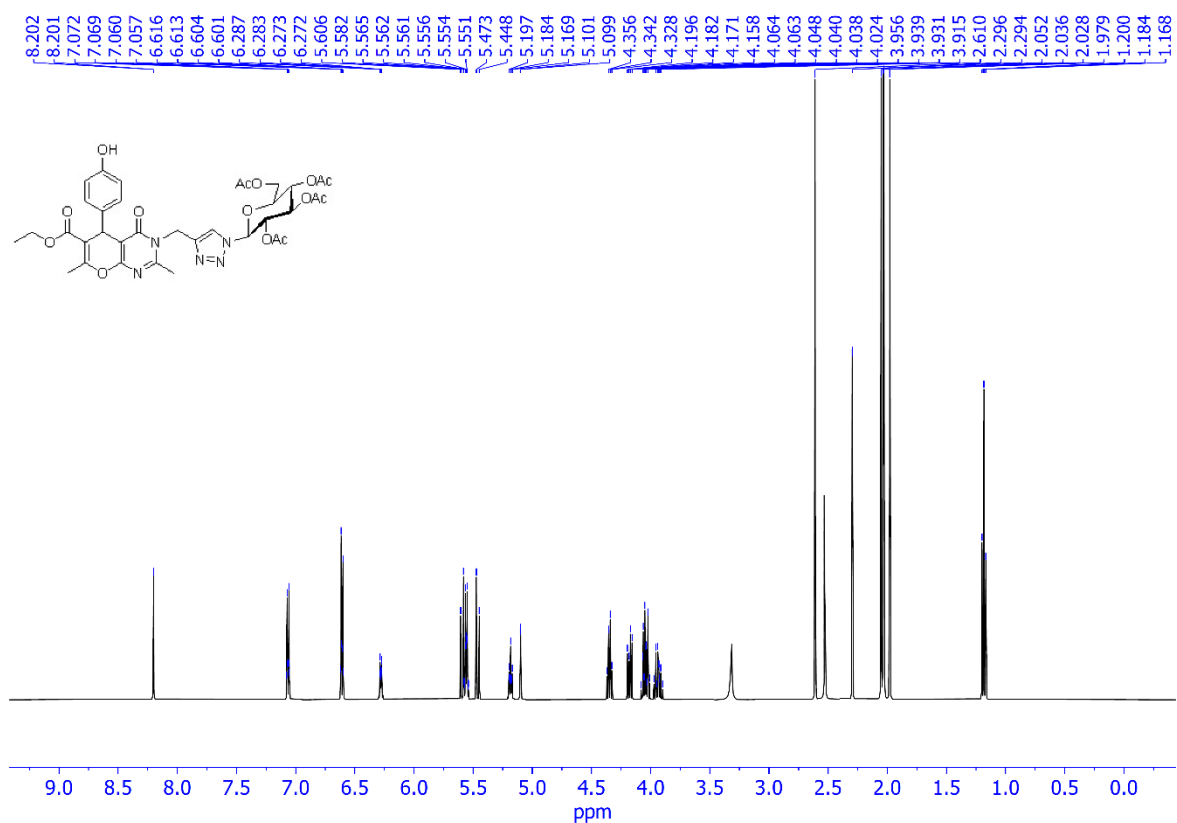


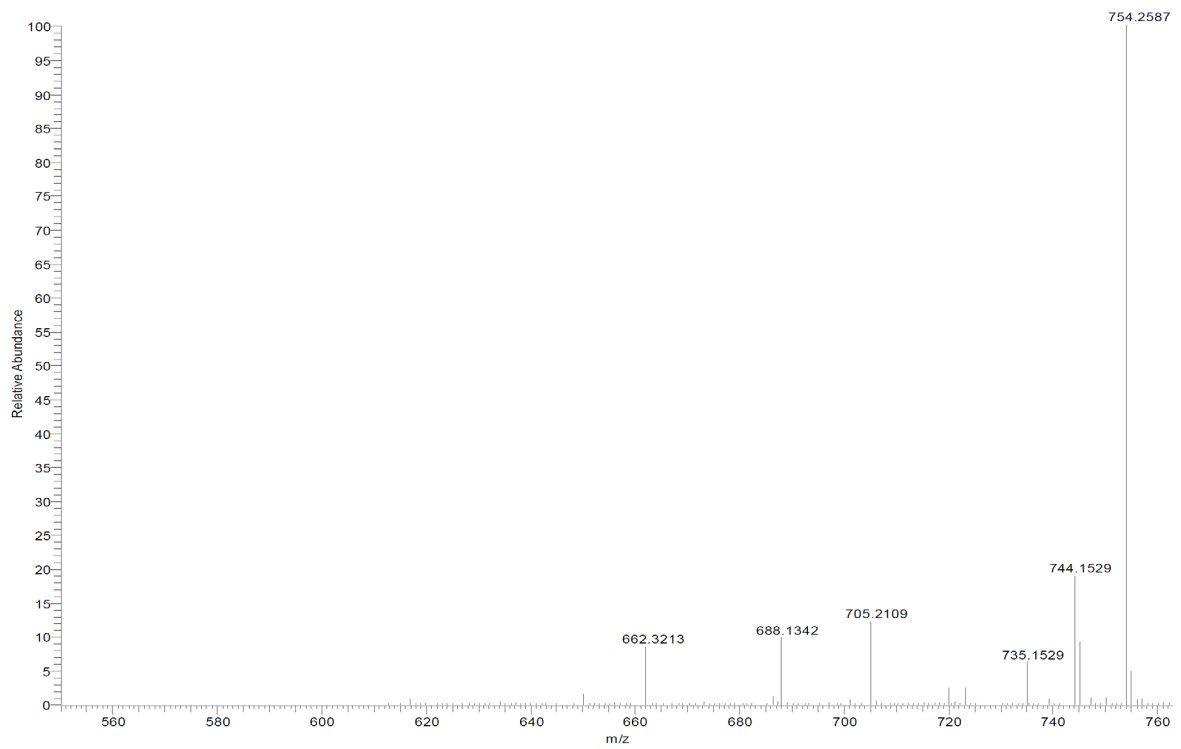
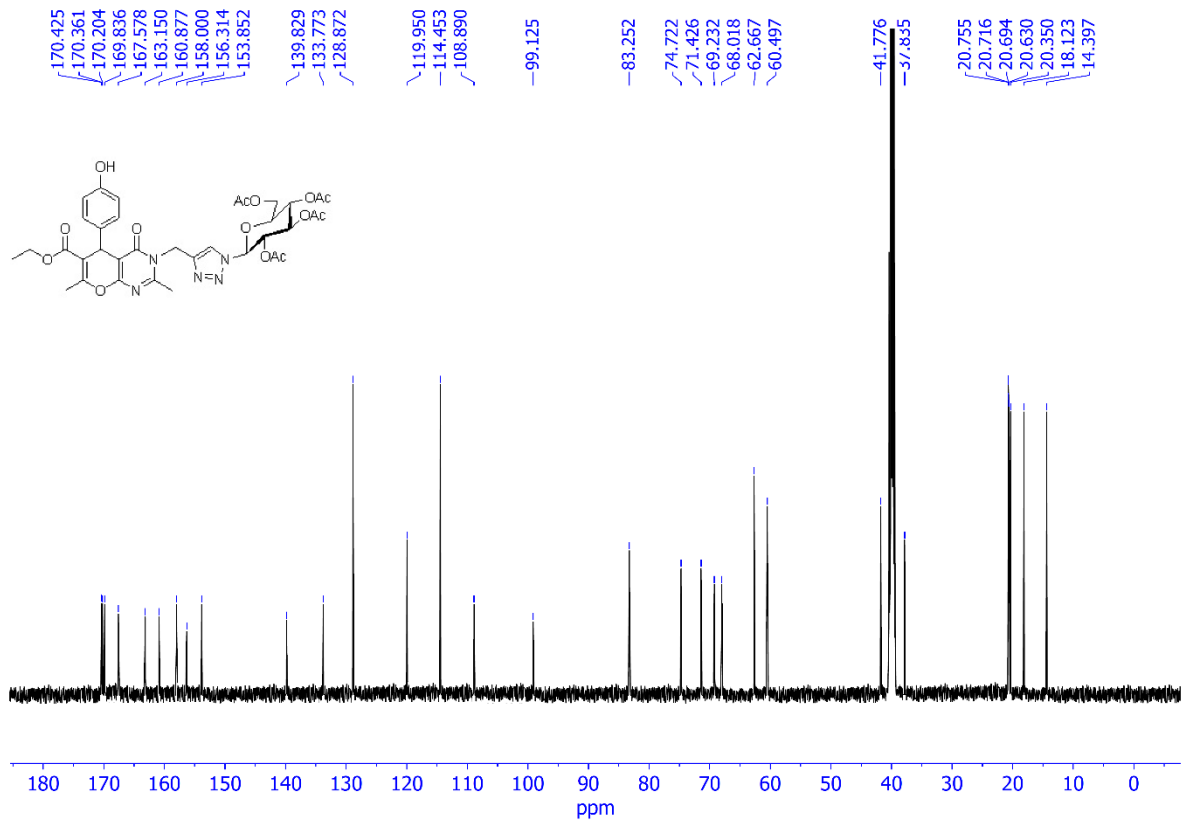
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-bromophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8h)*





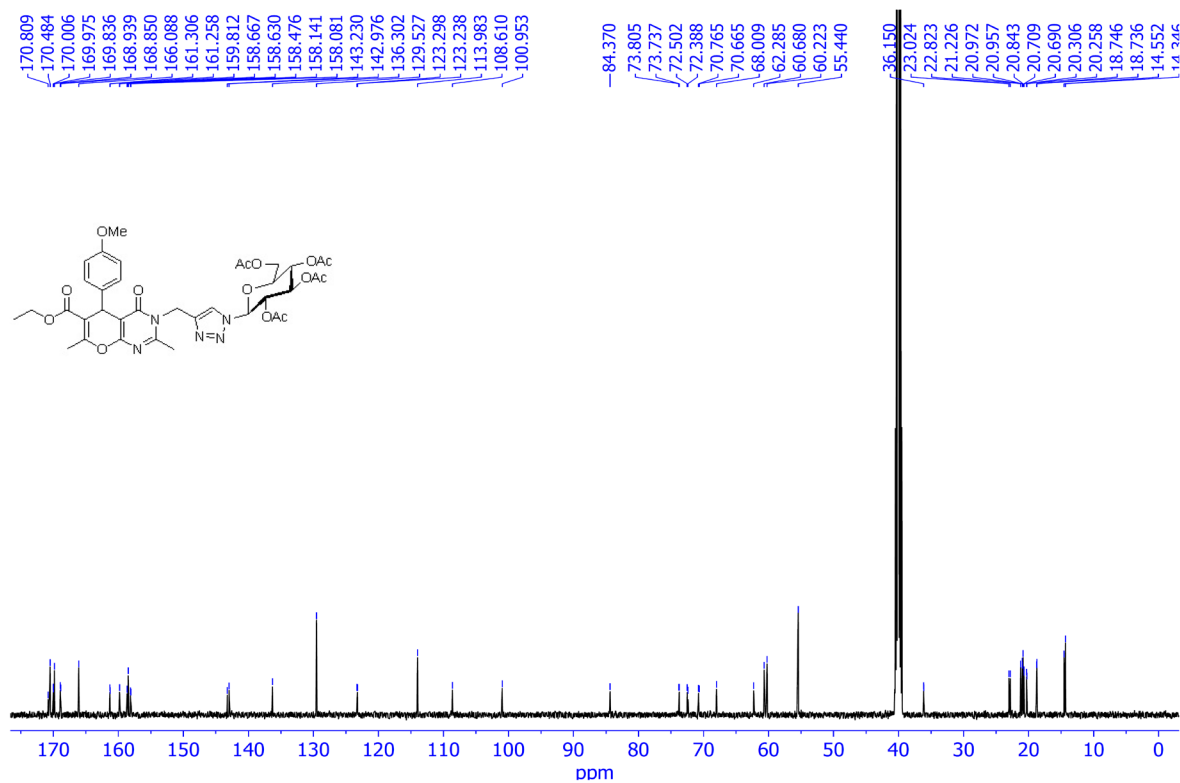
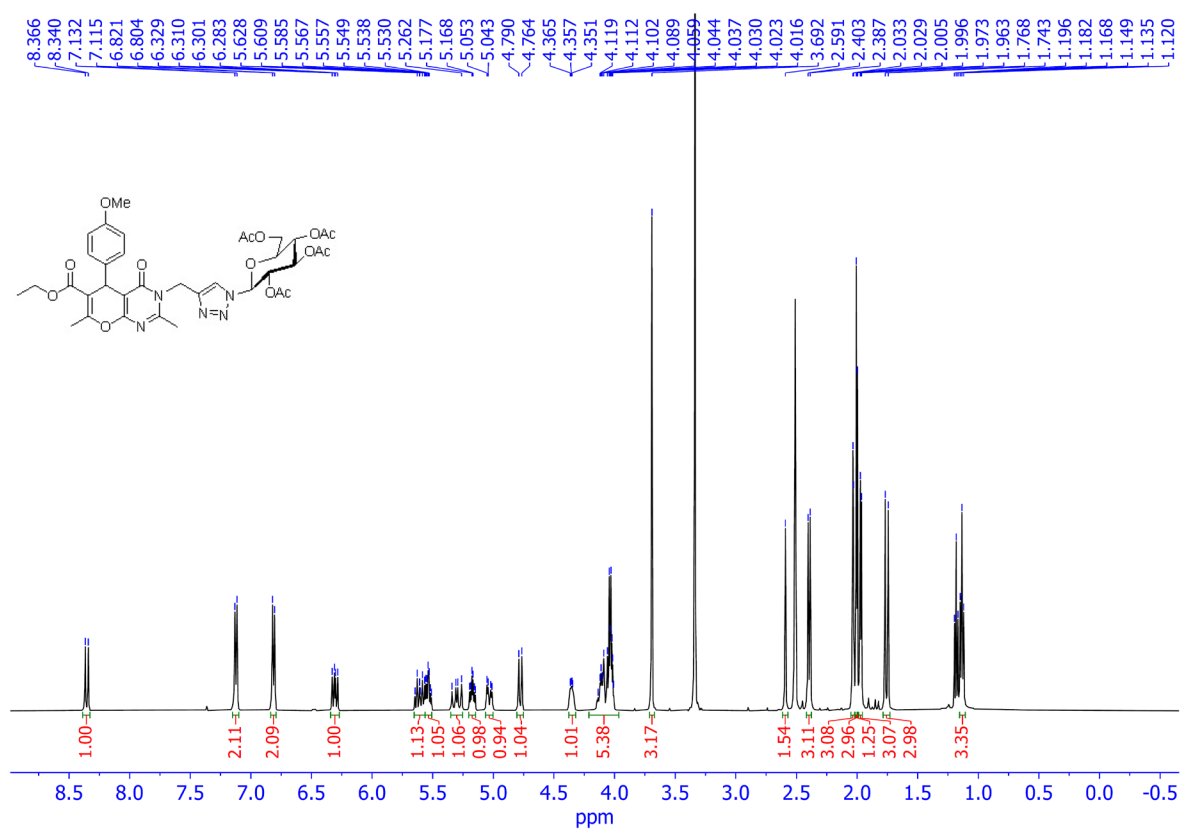
*thyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-hydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8i)*

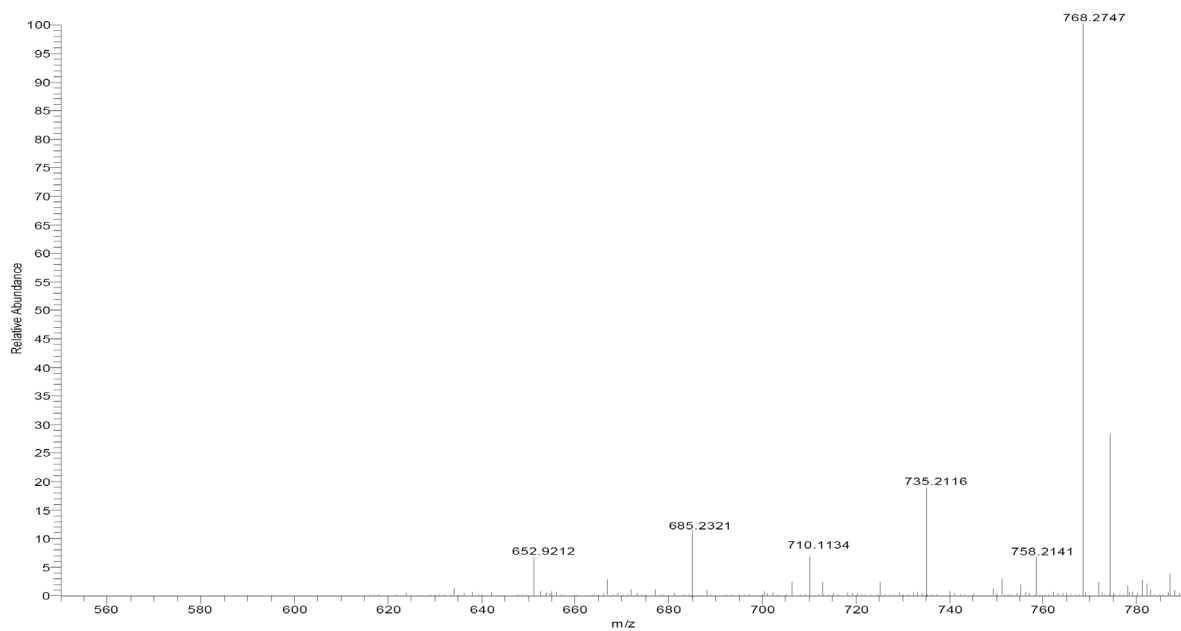




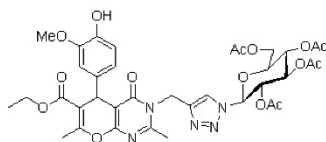
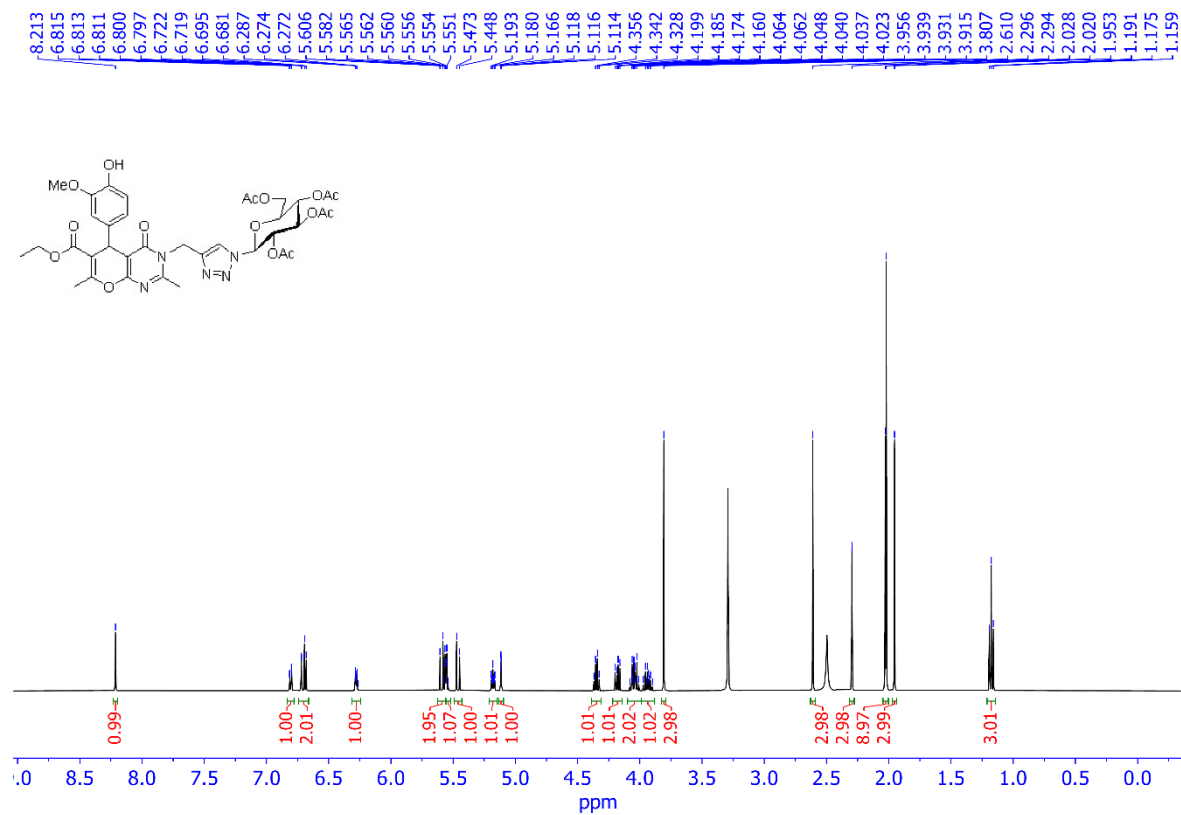


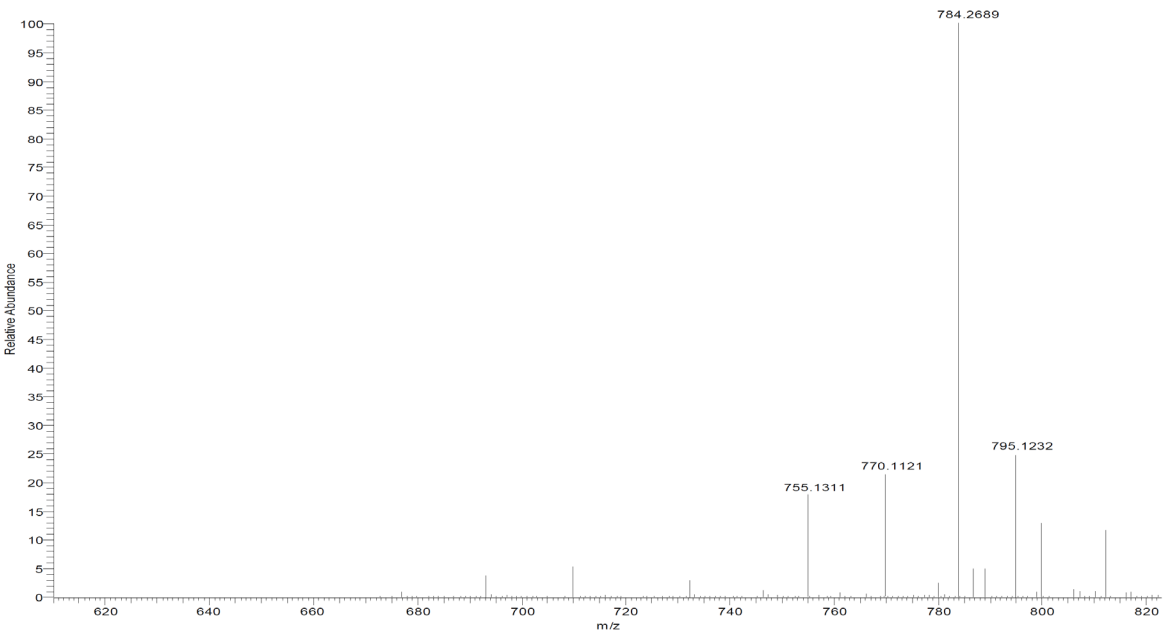
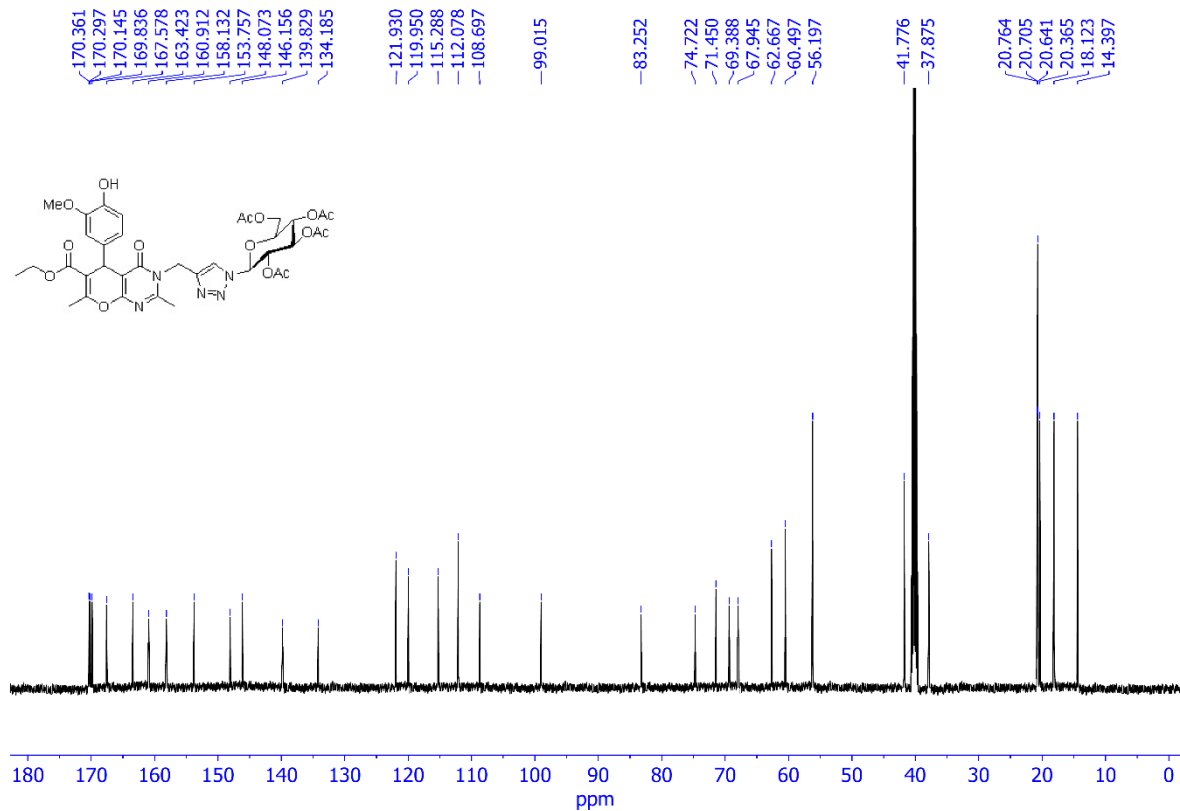
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate*  
**(8j)**



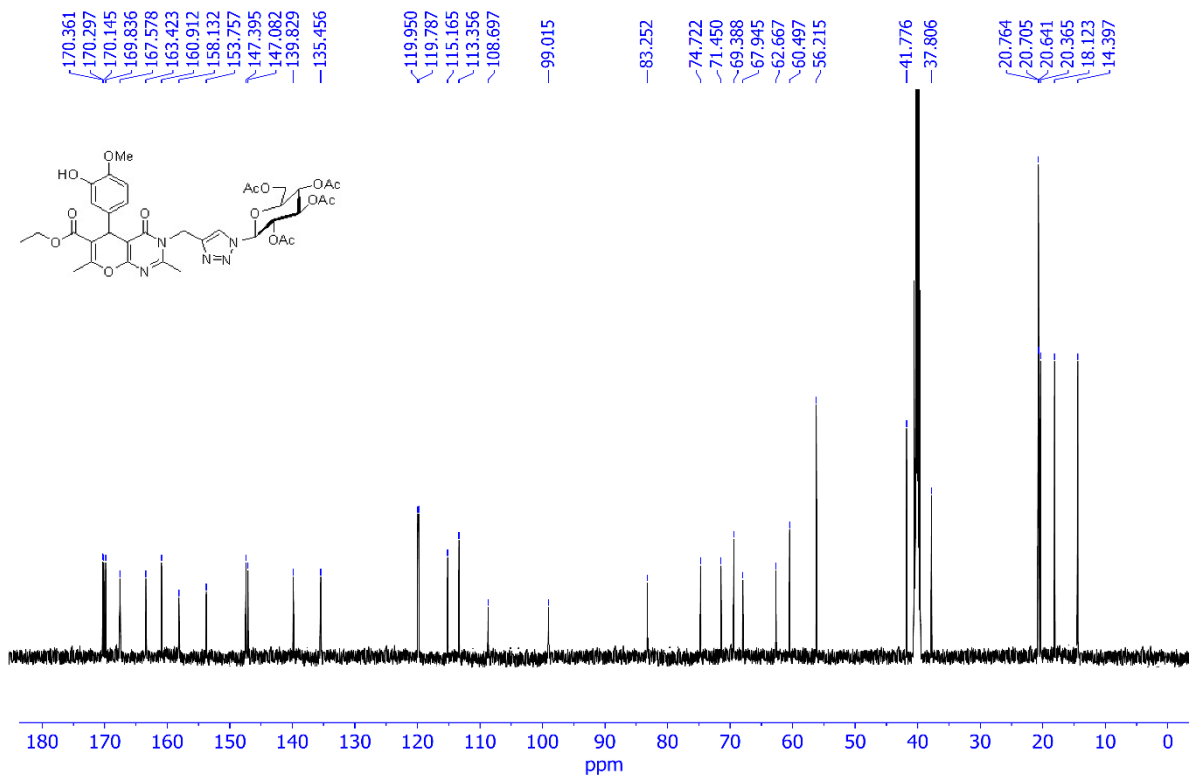
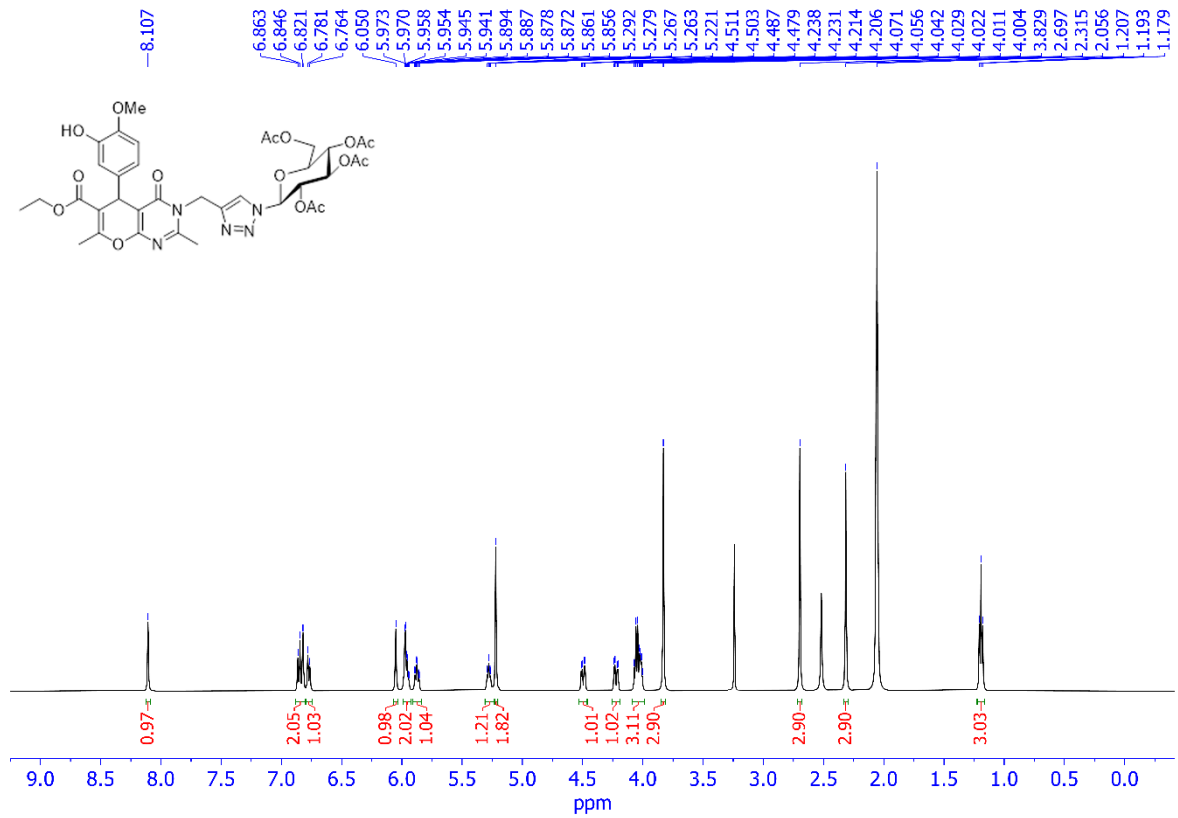


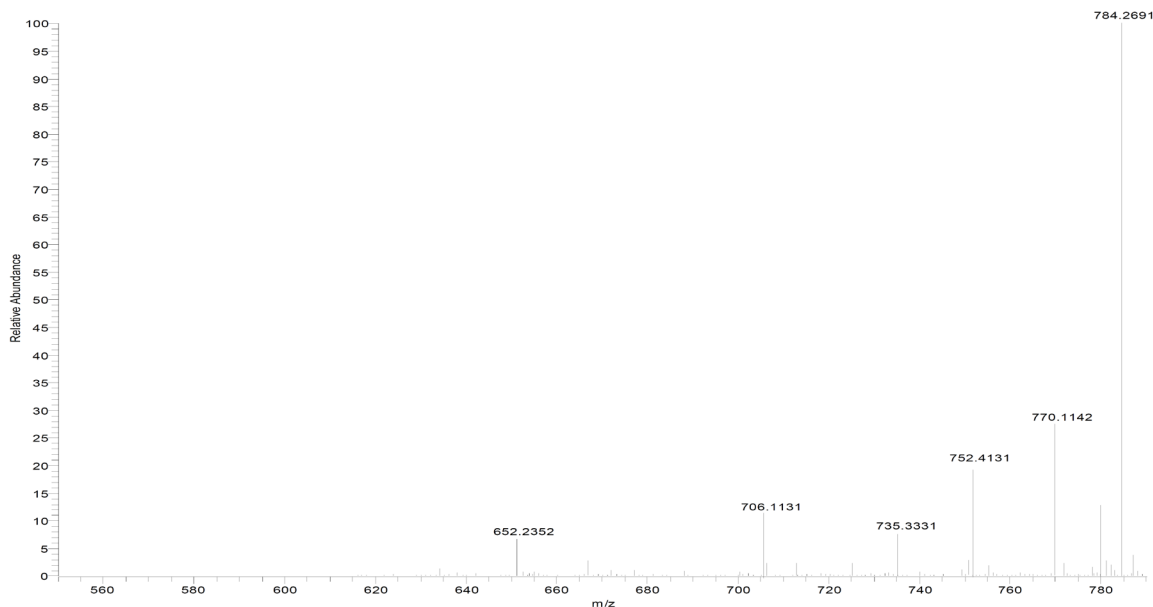
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-hydroxy-3-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8k)*



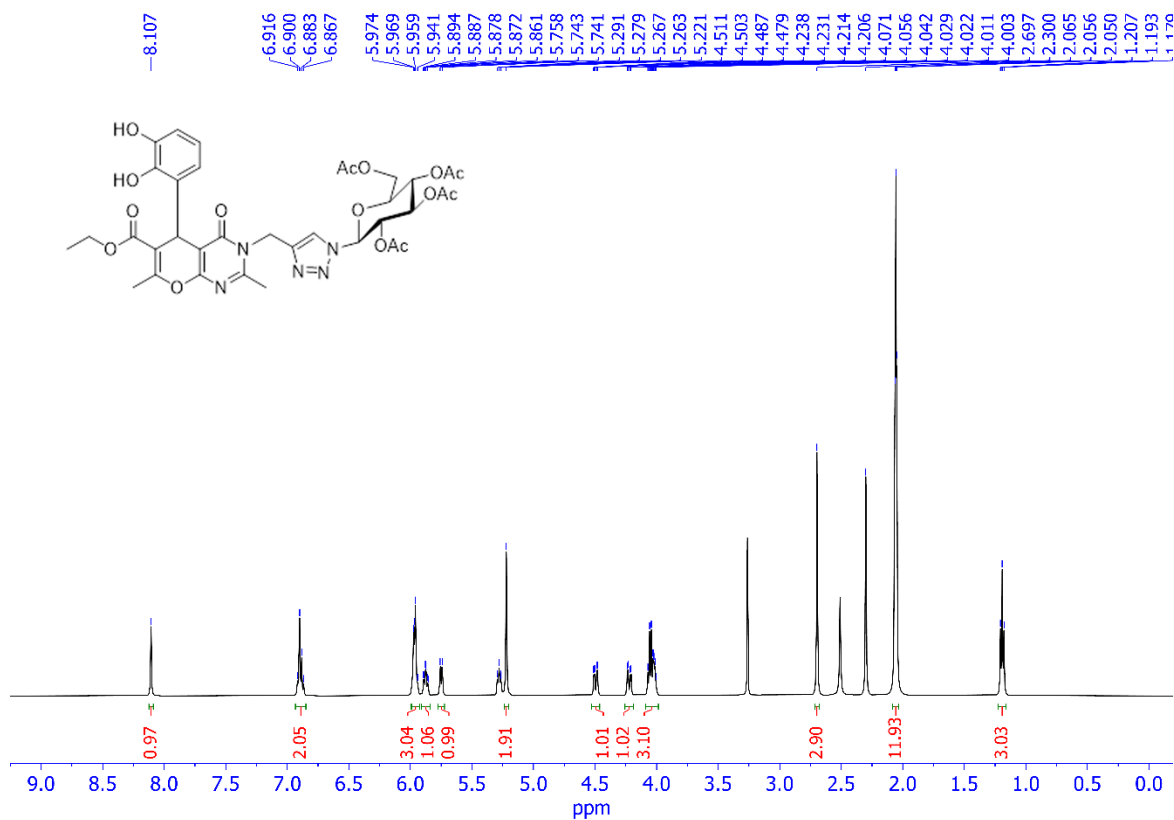


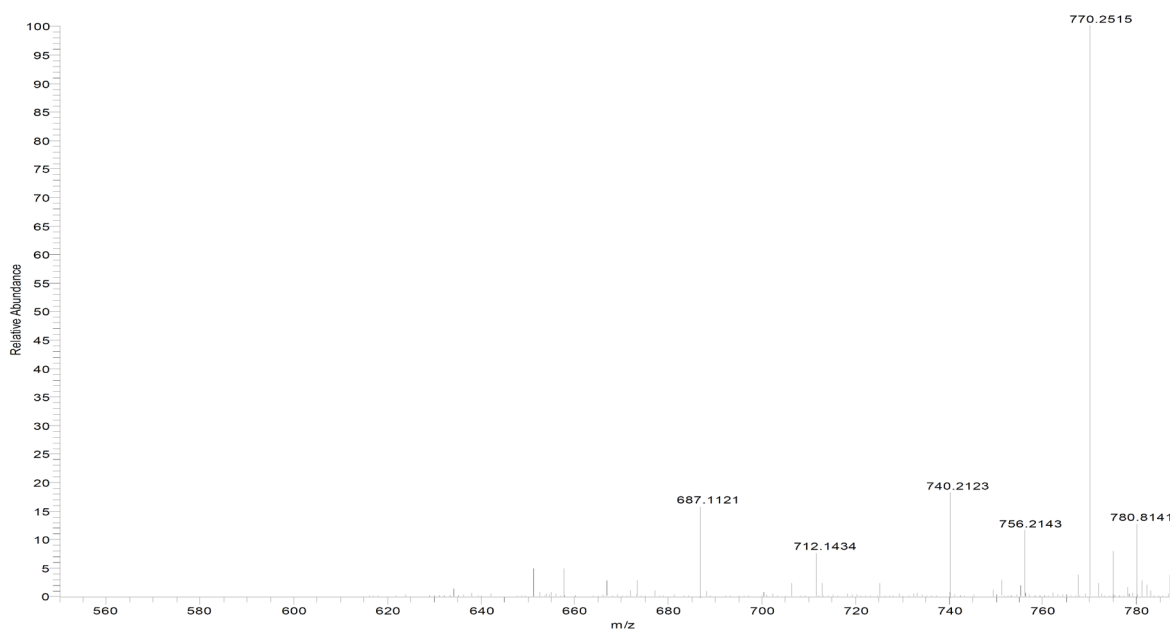
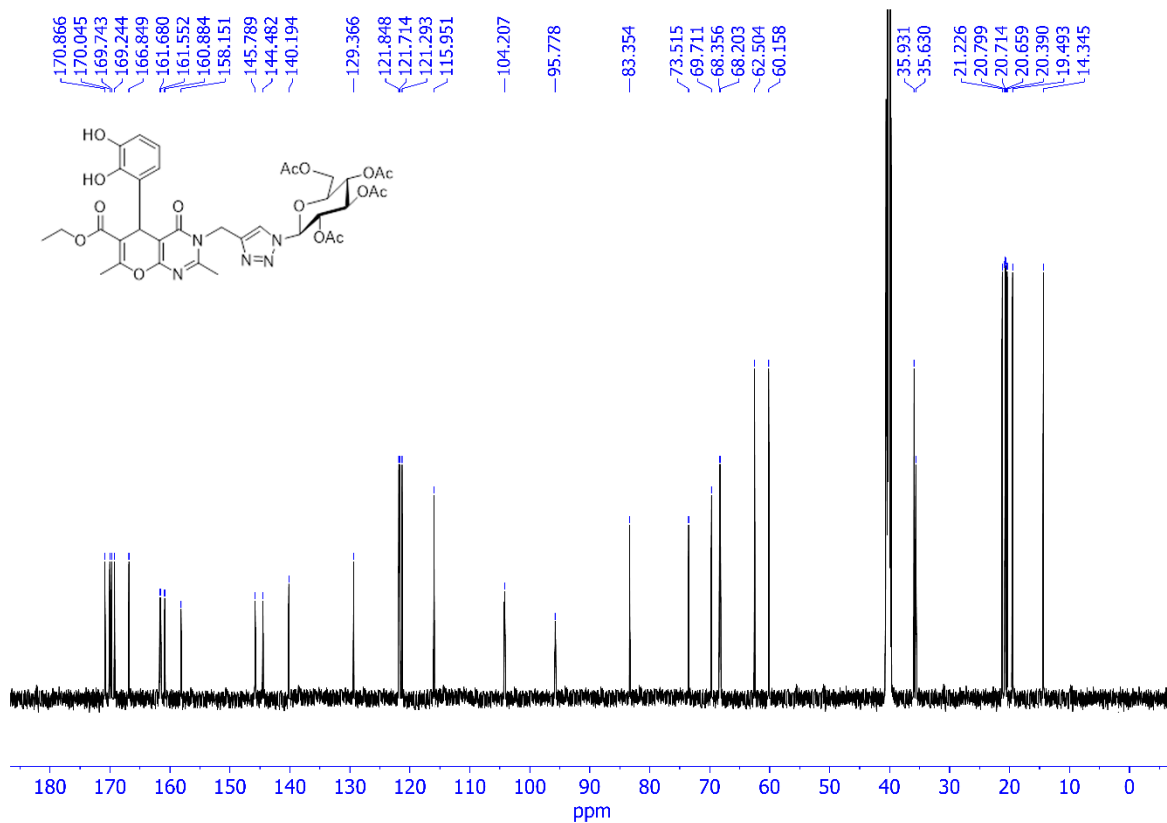
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(3-hydroxy-4-methoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8l)*



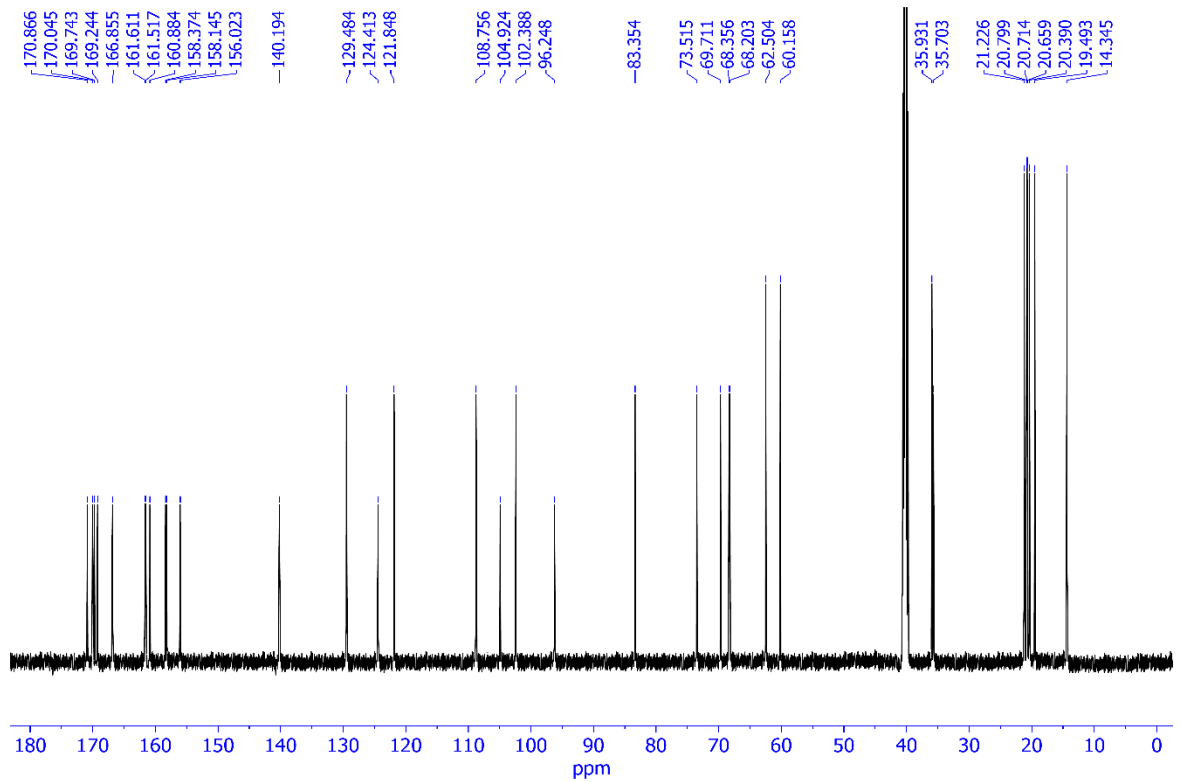
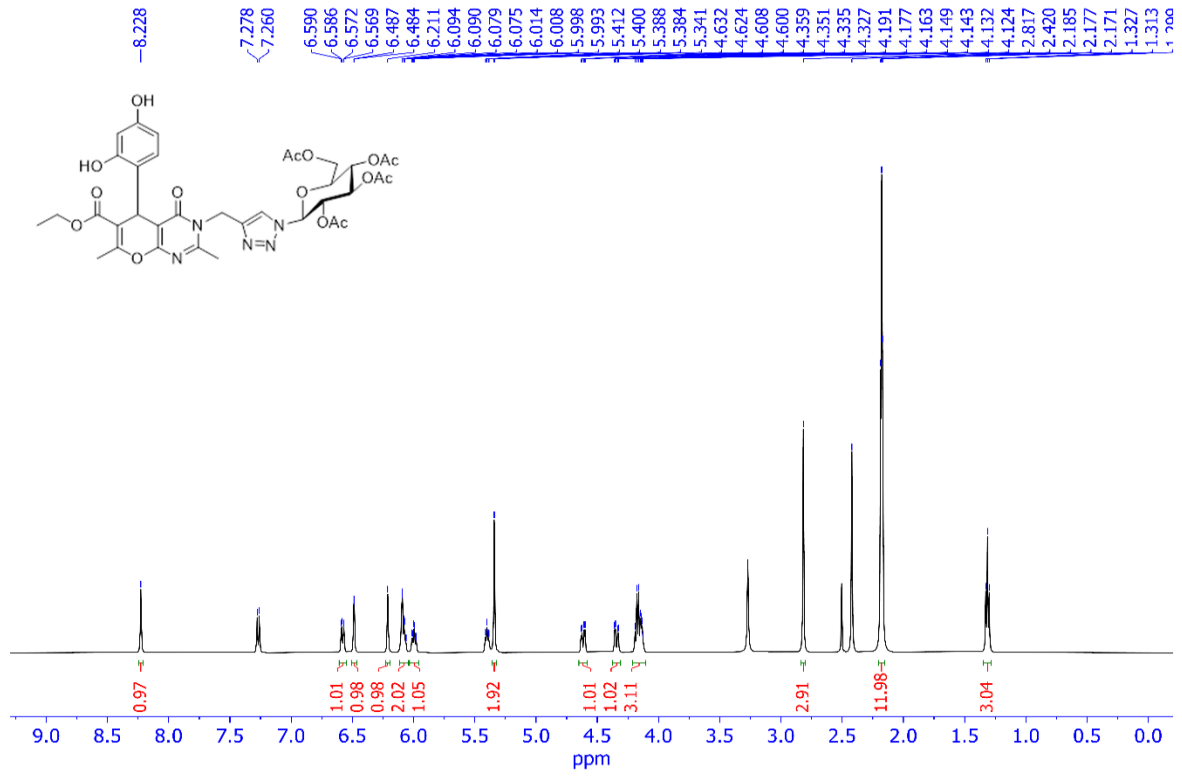


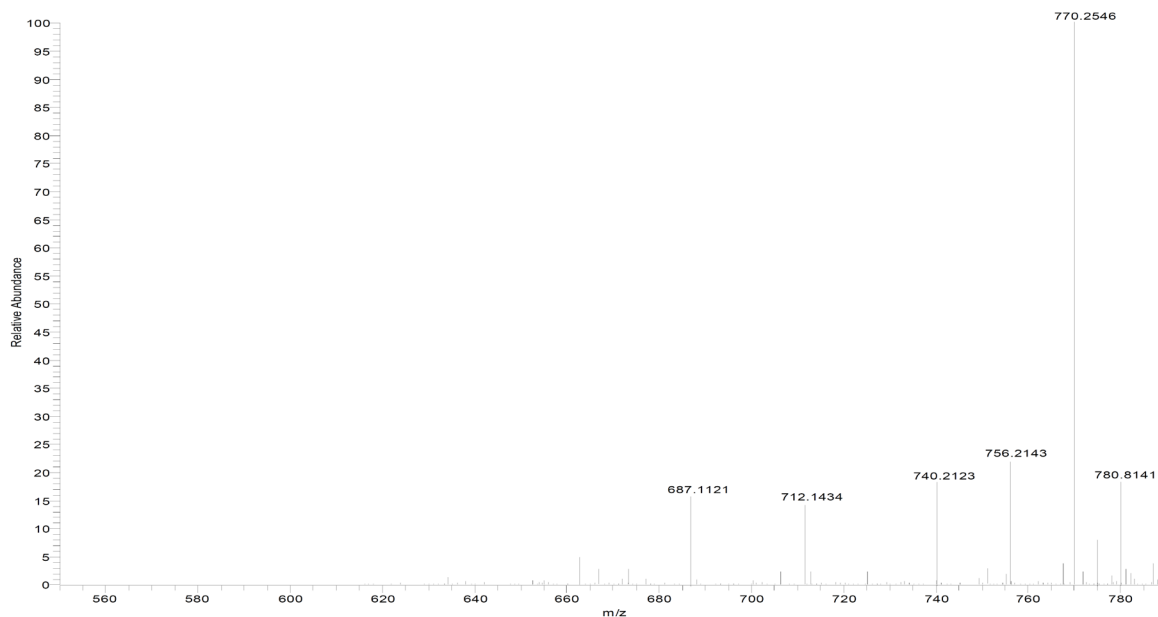
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2,3-dihydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (**8m**)*



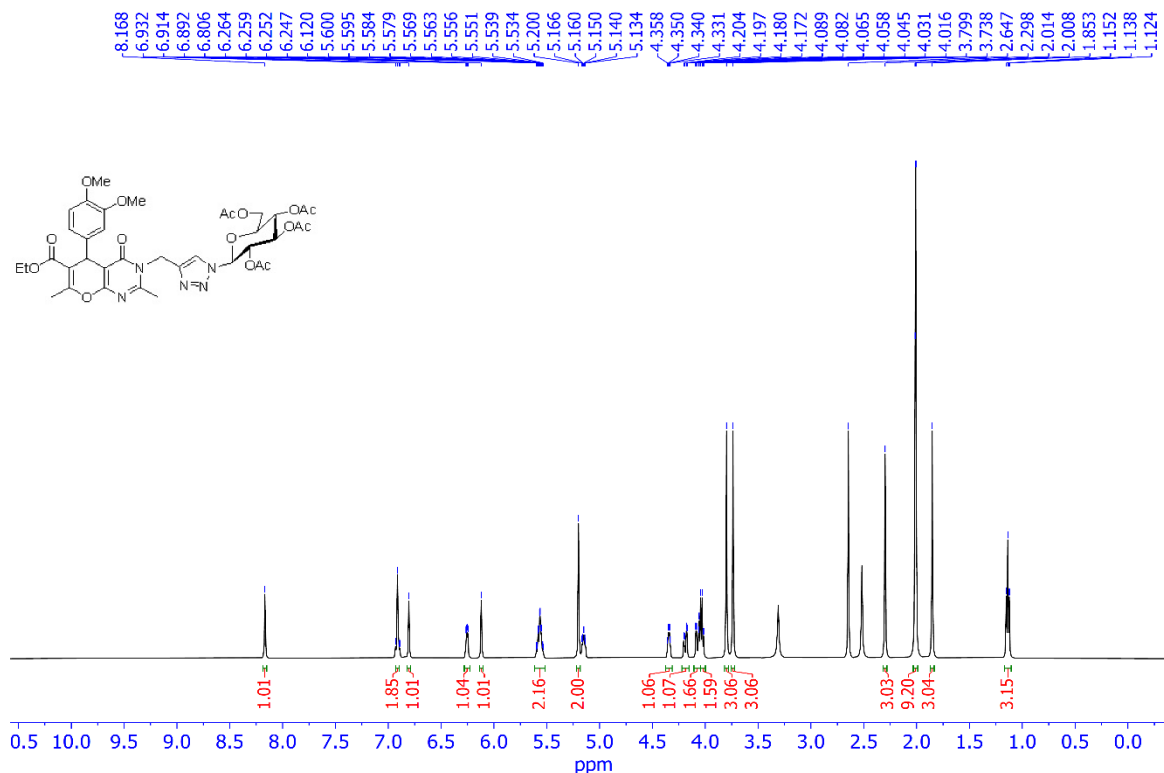


*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2,4-dihydroxyphenyl)-4-oxo-3,5-dihydro-4H-pyrido[2,3-d]pyrimidin-6-carboxylate (**8n**)*

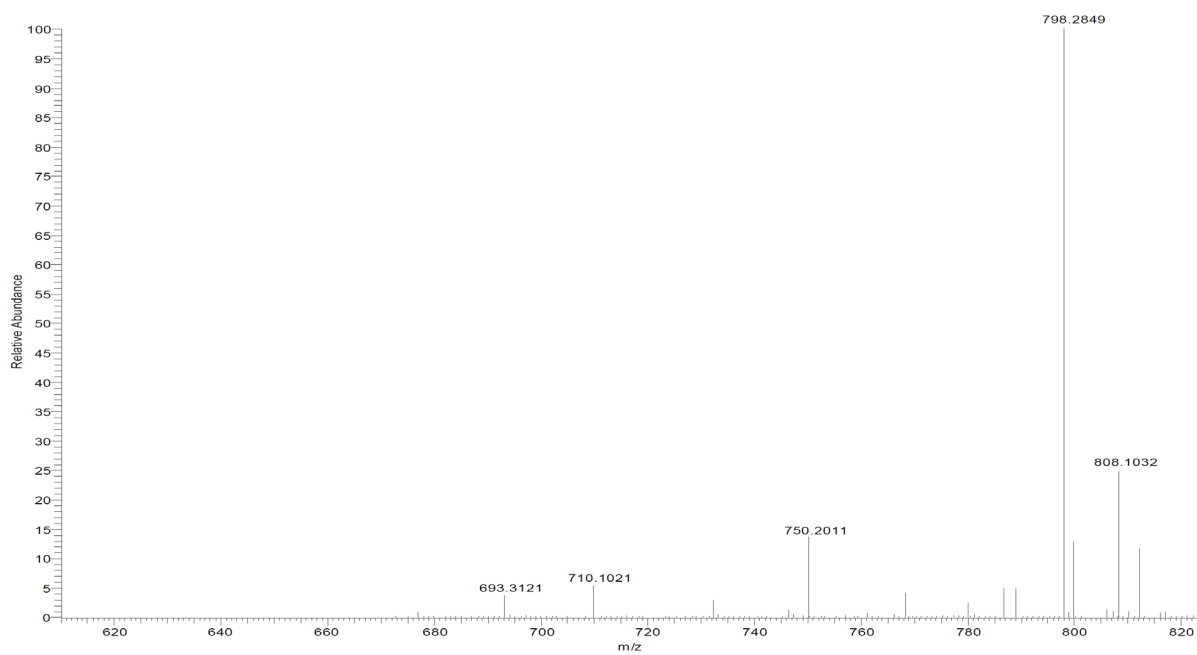
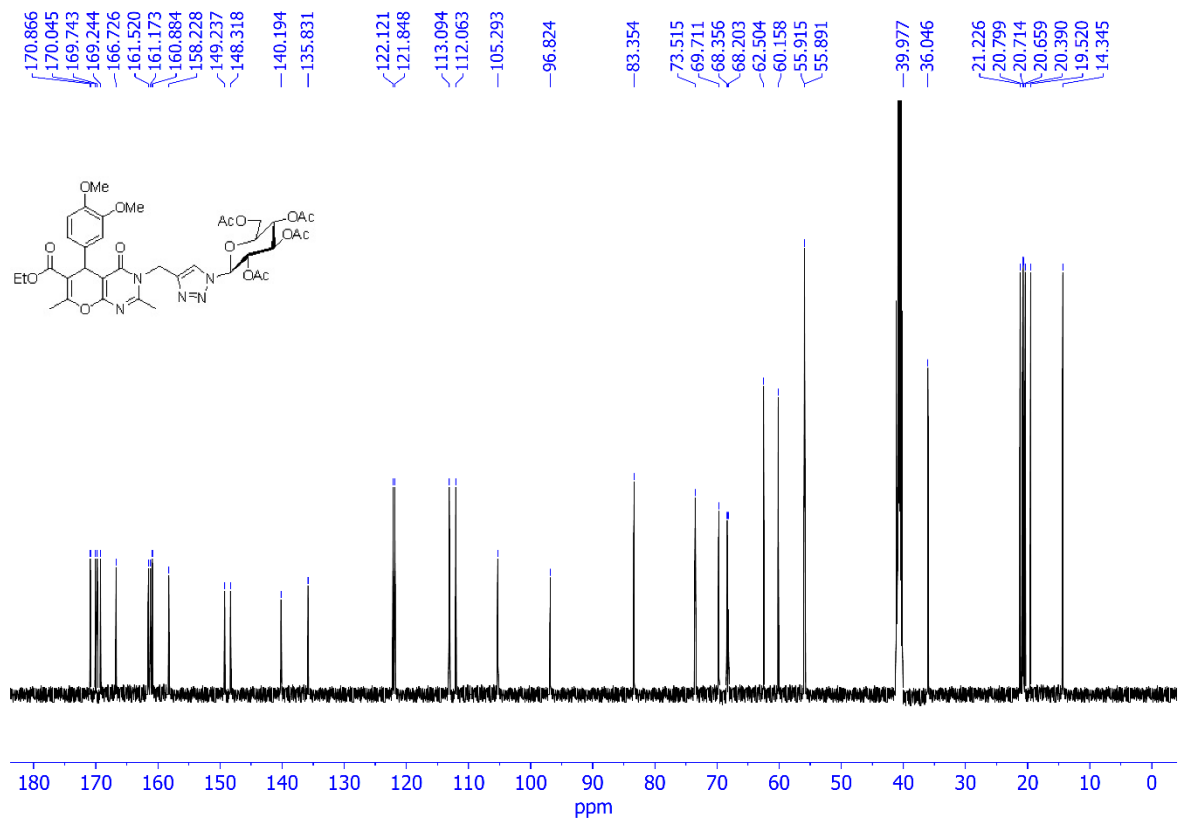




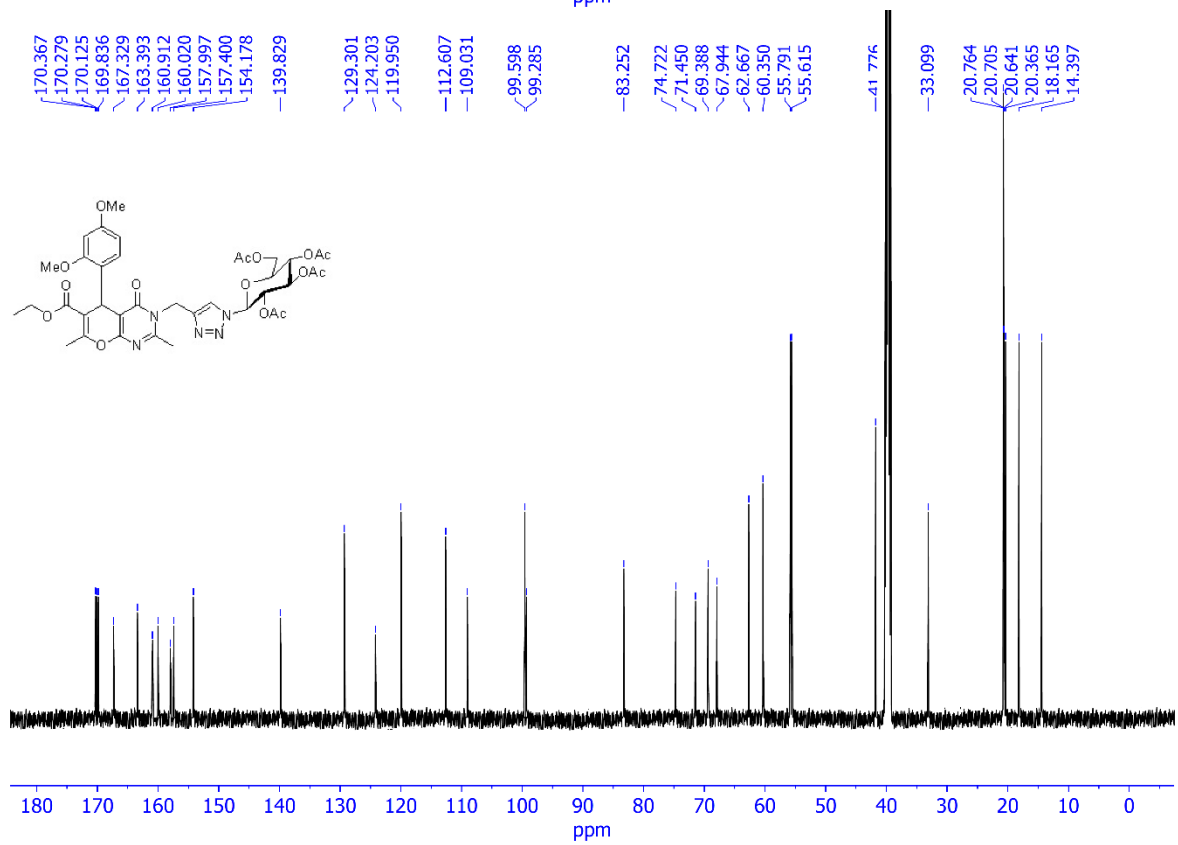
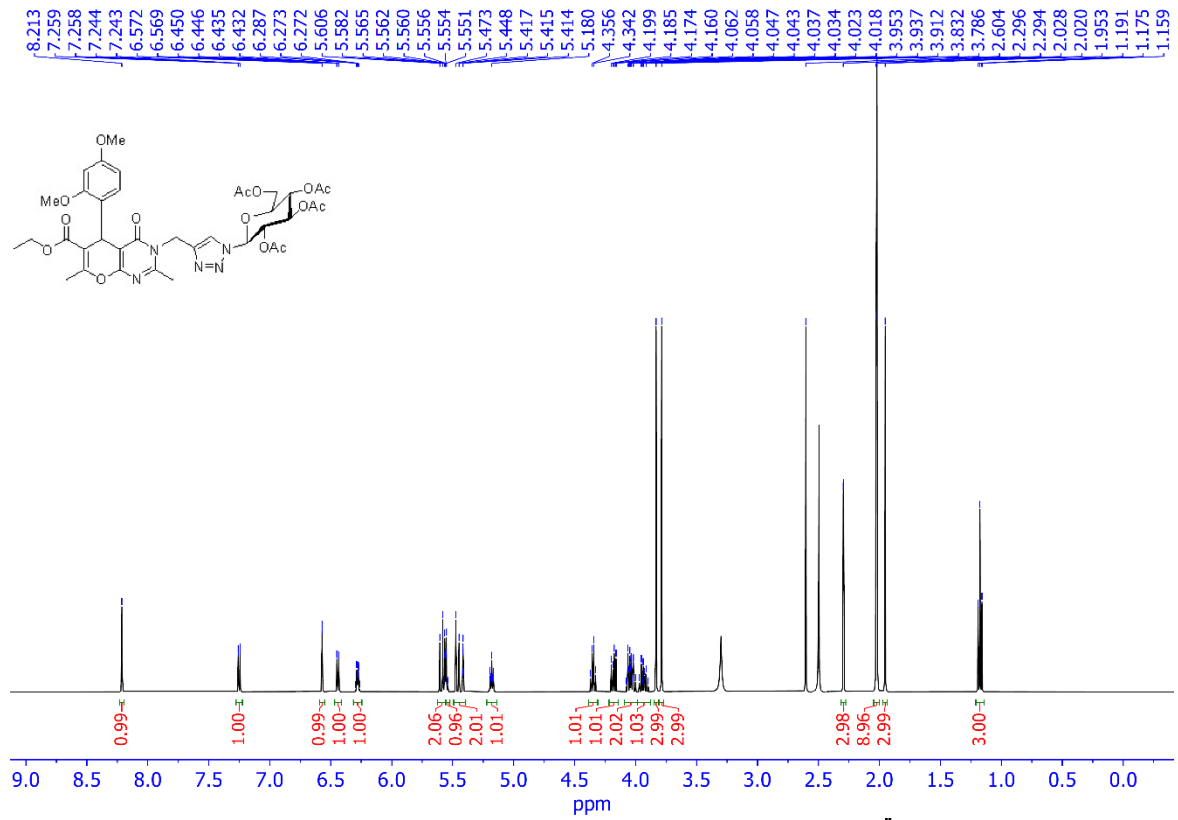
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(3,4-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (80)*

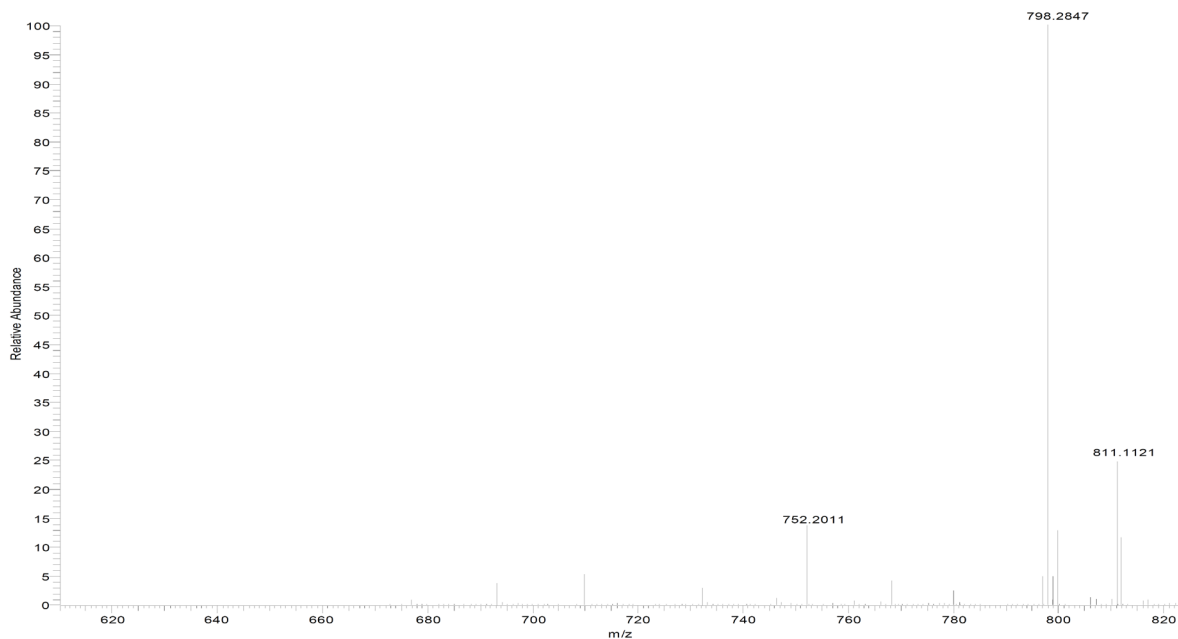




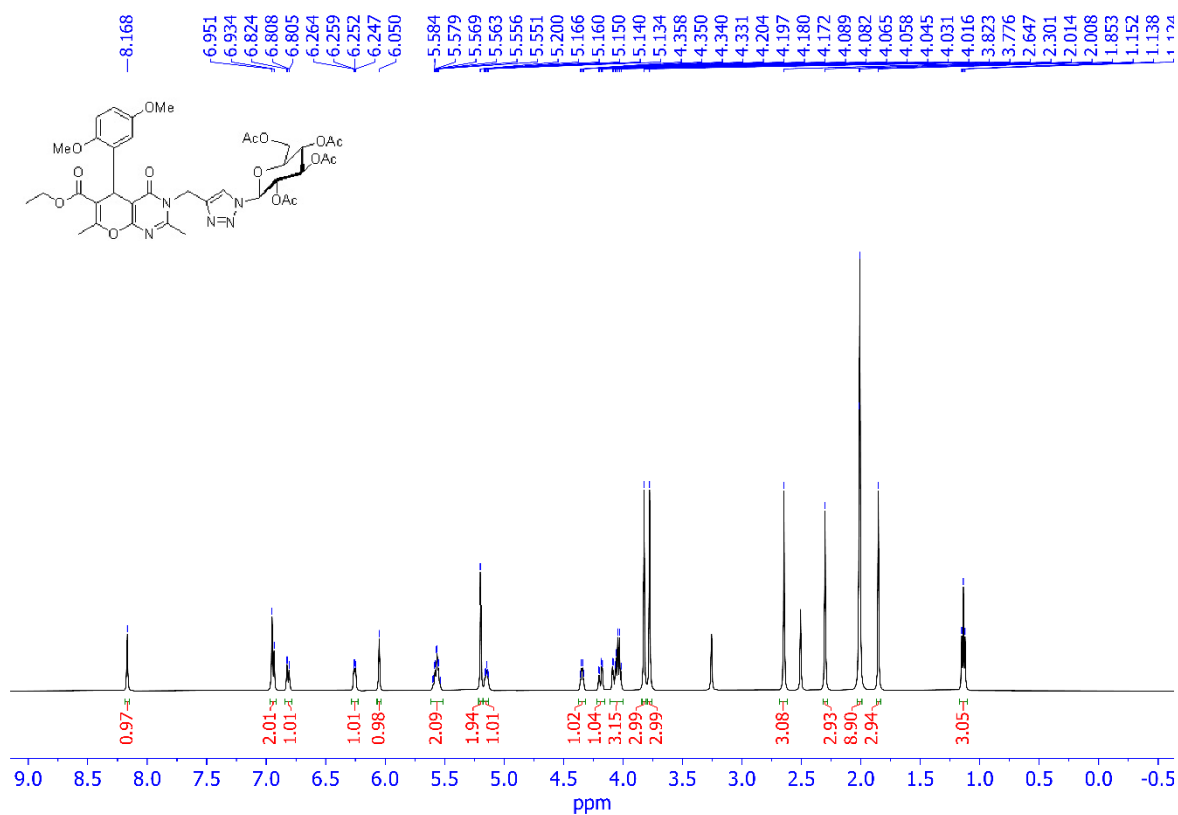


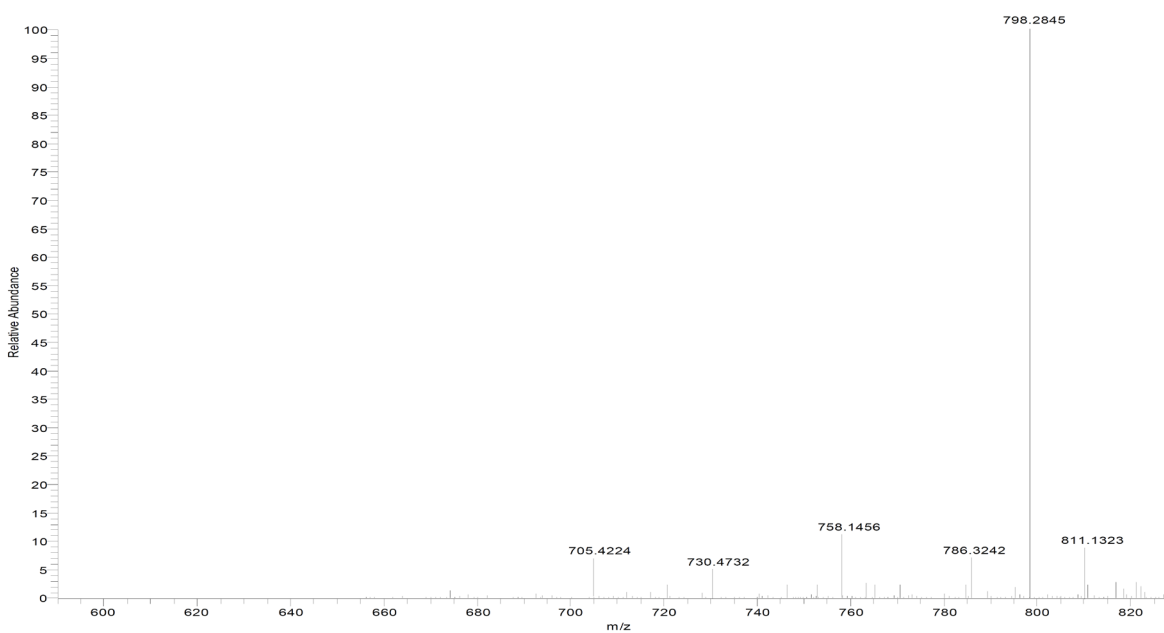
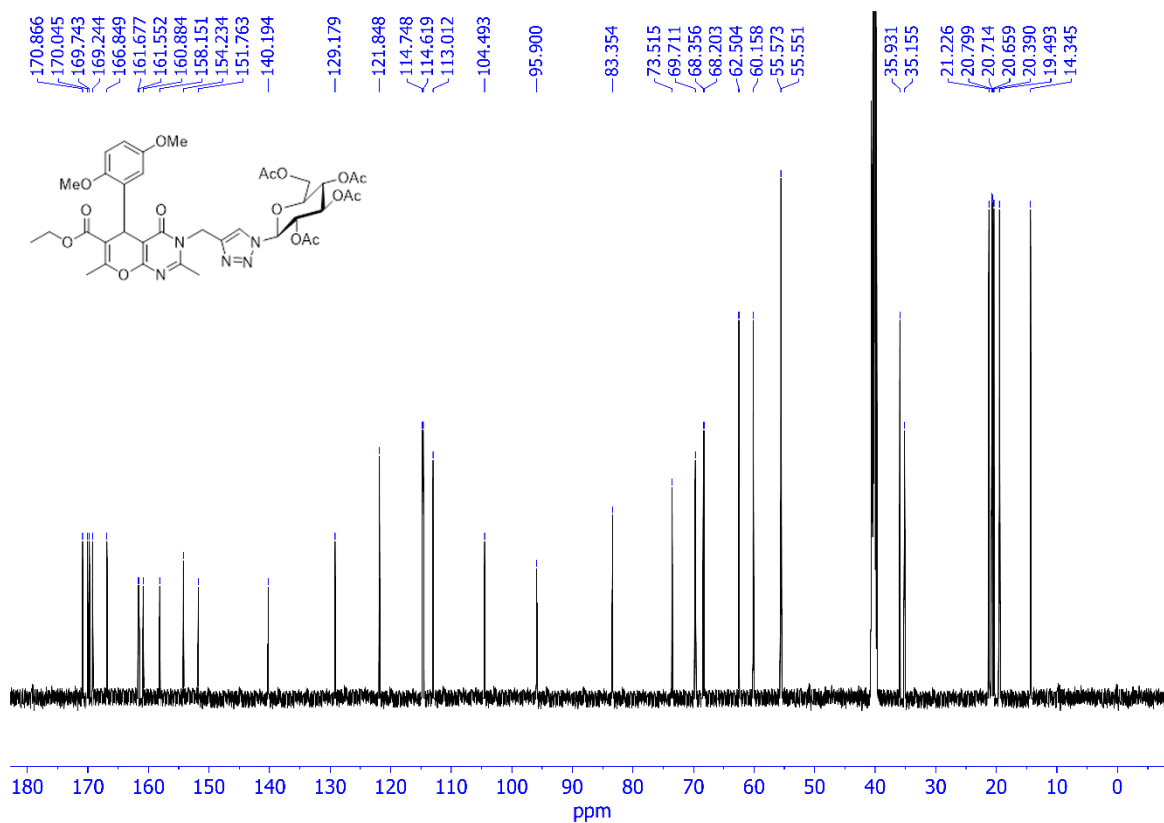
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2,4-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8p)*



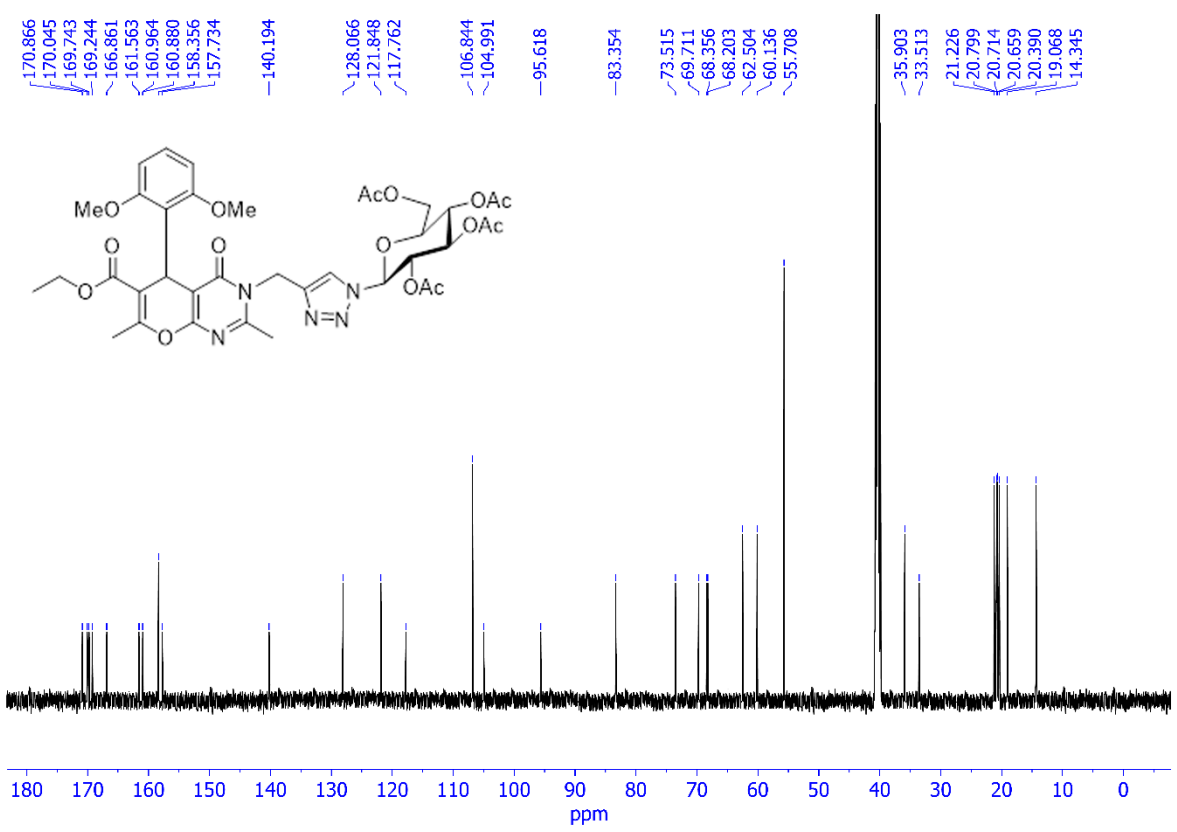
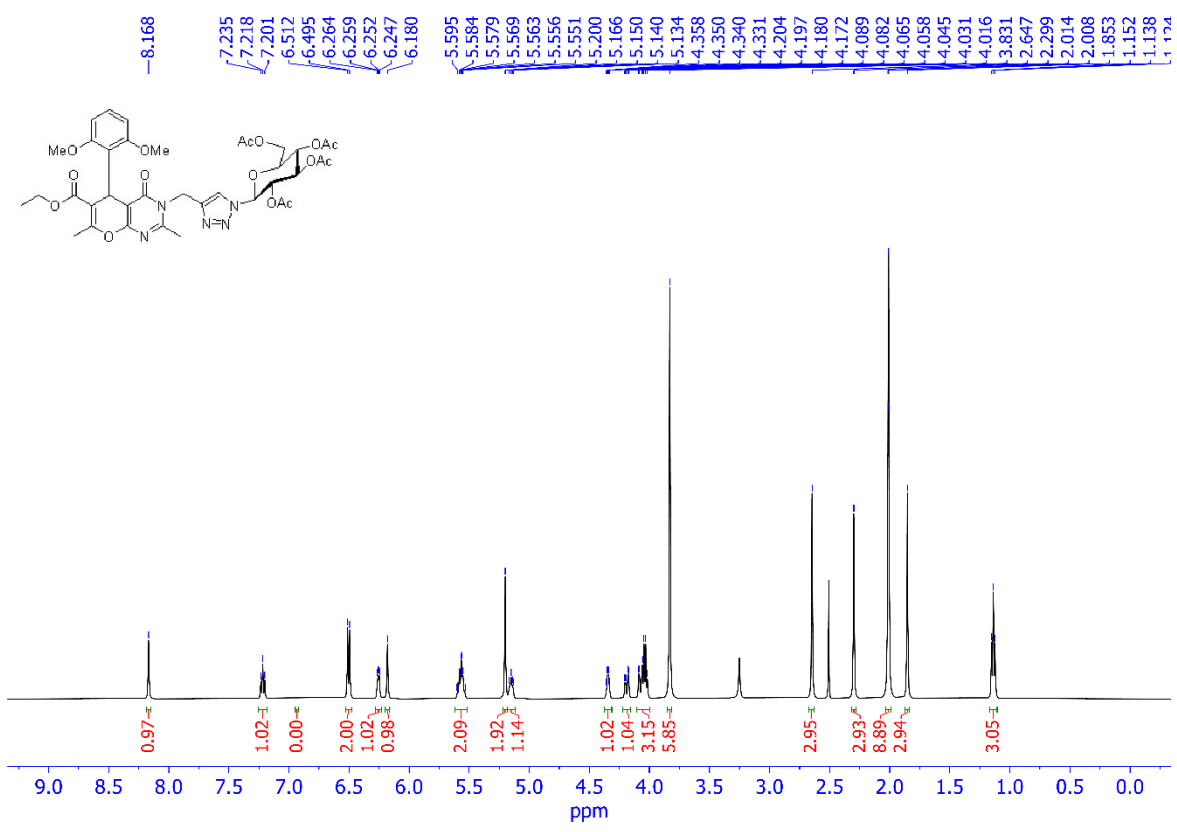


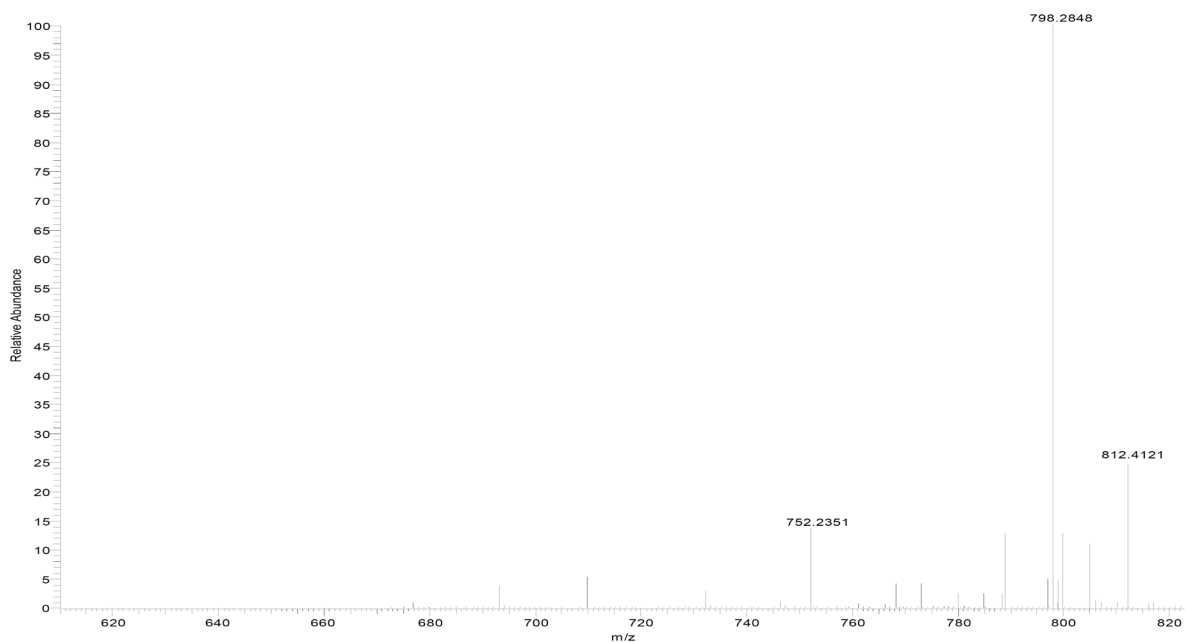
*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2,5-dimethoxyhenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8q)*





*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl- $\beta$ -D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(2,6-dimethoxyphenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8r)*





*Ethyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(4-dimethylaminophenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylate (8s)*

